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# WOMEN WAR CAPTIVES IN RUSSIA

BY

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In August, 1948, 24 women who had recently been released from camps in Russia were admitted to one of the hospitals in the British zone of Germany which received returning prisoners of war in need of medical care. They were, on the whole, in very good clinical condition, and this seemed remarkable when considered in relation to the known or generally believed stories of hardships of life in Russia. It was therefore decided to obtain from some of the women careful and detailed accounts of their experiences.

In order that the accounts might be comparable and more easily managed, a questionary was drawn up and was followed as closely as the women's talent for diversion allowed. The account now presented was put together from the replies received. So far as possible it is an exact record of the replies, and comment has been excluded.

Six women, whose ages ranged from 21 to 37, were chosen for the questioning. They were all women who had come to the British zone as *Ost-Flüchtlinge*—that is, they no longer had any homes in any of the four German zones. They were questioned in complete privacy by a woman doctor who spoke German and English fluently, and they gave the accounts of their lives in Russia with perfect willingness and, so far as could be judged, without exaggeration of their hardships or pleasures. They appeared to be excellent witnesses, and their statements, made without hesitation and quite spontaneously, bore the ring of truth. The frequency with which they corroborated each other's stories was extraordinary. Two of the women (Margret and Ida) were, in fact, discovered to have been inmates of the same camp by the exactness of their descriptions of camp conditions.

### The Women, and How They were Taken into Captivity

The six women were Ida and Elli, both aged 21 ; Hanna, aged 24 ; Margret, aged 26 ; Agnes, aged 32 ; and Emma, aged 37. All six came from the eastern portion of Germany, which is now partly Russian, partly Polish. Hanna came from the south (Silesia) and all the others from the north (Pomerania ; East and West Prussia). They had all lived in country districts, and all except Hanna, who worked in an office, were doing housework and farmwork in their own homes. The two eldest women were married. Agnes had a daughter aged 12, but Emma had no children. Agnes's husband had to join up in 1942, and she then went home to her mother ; Emma's husband, who was also a soldier, was reported missing in October, 1944.

The villages in which the women were living were occupied by Russian troops in February and March, 1945 ; and shortly after the occupation Elli, Hanna, and Margret were visited by soldiers, who told them to go away with them immediately for three days' work. Elli, who had been expecting a summons of this kind, was wearing extra clothing and was told to take a blanket with her. Hanna was caught when on a visit to the neighbouring town. There she was questioned extensively, then taken to her home and told to dress in her warmest clothes. Margret had a rucksack, in which she packed some warm garments. Ida was taken from her home and told she must work for four months, and she also was allowed to pack a bag with some clothing. Agnes would have been taken from her home in the same way, but the Russians who came for her were apparently unnerved by the screams of the children who saw her going. Next day, however, while she was at some compulsory work of clearing away rubble, she was arrested with the women who were working with her and given no chance to go home. Emma hid in her mother's home for fourteen days after the Russians came, and then went with other women to the Russian commandant to ask for work, which they hoped might provide them with some sort of protection. They were set to mind horses. After a fortnight of this Emma was taken to the next village to clear away rubble. She could send no word home, and did not, in fact, see her home again.

It appears that to some extent age determined the choice of prisoner. Thus Elli and her sister aged 15, and four girls of similar ages, were taken together ; Margret's father (49), her sister (20), and her brother (18) were taken with Margret herself, but her two sisters (13 and 7) and her mother were left. There was at this stage no examination to determine fitness for work. All the six women knew of cases of women who were pregnant when they were taken off. One gave birth on the journey to Russia, and she and her child died. Many others whose children were born later were repatriated after a short time.

### Conditions on the Journey

It was usual for the women to be collected in cellars or other safe places. When the numbers were sufficient they were either marched or taken by lorry to a railway centre ; a period of from seven to 14 days was usually occupied in these preliminaries, and all the six women said that it was physically the most exhausting of their experiences and the most severe mental strain. There was a widespread fear at this time, which seems to have been to some extent justified, that they were in constant danger of rape. There was no actual corporal punishment on the march, but the guards were very strict, urging the prisoners on with their rifle butts. Some of the women had to cover

long distances. For instance, Elli had a very hard journey. Her party was forced to walk for the first two days, and many of the women broke down and were left by the wayside, and Elli does not know their fate. The night of the second day was passed at a farm, where they were offered good food but were too exhausted to eat it. The next day the party were lodged with about 2,000 other women in a bank building, where they were kept for two days. On the third day they set out on a journey in which they walked 100 km. in three days. Many fell out, and the officer in charge said: "If you cannot get along, stay here and go '*kaput.*'"

At the railway centres it seems to have been usual to provide washing facilities, and something was done to eliminate lice. For the actual railway journey into Russia the women were packed into cattle-trucks, about 80 in one truck. Sleep was very difficult, and if one woman wanted to lie down, other women had to stand. For toilet purposes there was a hole in the floor of the truck. Washing was impossible, and the food was very inadequate; a little bread was distributed three times a day, and each woman had one spoonful of sugar a day. All six women agreed that the lack of water was, however, the worst of their deprivations, and Elli and Emma said that their parties were actually screaming for it. One girl aged 18 in Elli's truck died after having diarrhoea. Elli thought that about 40 to 50 of the 2,000 women in her transport died on the journey. The train journeys lasted from two to four weeks; Ida and Hanna had the shortest journeys, and Elli the longest.

One woman, Hanna, ended her journey in the Caucasus, and the other women went to the Urals. The women all remained in these districts, but they were moved from camp to camp several times until they finally settled in camps where they stayed for periods lasting up to two years. In the Urals the variations of temperature between summer and winter were extreme, with cold in winter down to minus 50° C.; but in the Caucasus the climate was more temperate. The camp conditions in the first few months were obviously very bad. The camps usually consisted of collections of wooden huts, which were in a filthy condition and overcrowded. Many deaths occurred in these first months; Elli said that 18 of the prisoners with her died in one day, and she and the other women believe that the total number of women prisoners was almost halved by death by the end of 1945. The chief causes of death were typhoid and similar gastro-intestinal illnesses, and "water," which was apparently a generic term for swellings of feet, hands, and face.

### The Work and How it was Done

The first medical examination was made by Russian doctors, or by German doctors under Russian supervision, within three to four weeks of arrival. The women were classified according to their capacity to work, but the examination consisted merely of an inspection. There was no thorough investigation. They were put in four groups: Group I were the fittest, and Groups II and III were less fit but still capable of work, whereas those in the fourth group, called "O.K." (*ohne Kraft*), were unfit for anything except cleaning and other chores in the camp. Margret and Emma were classified at this preliminary examination as "O.K." and the others as Group II.

Margret and Emma had no set work for the first six months. Agnes was put to work in a lime-kiln, and her job was to fill trucks with the lime. She said it was very hard work and the lime made her eyes smart; other women had lime burns. Ida, and Margaret as soon as she was well enough to be put in Group III, worked in a peat-field, carrying the turves, stacking them, and loading them into trucks. The actual cutting of the peat was usually done by men or by the fittest women. Elli worked in a coal mine 275 metres below the surface. There she had to drag pit-props a distance of about 700 metres. The mine tunnels were only about 1.5 metres high, so that she had to walk in a bent position. For a short time she had to shovel coal. Hanna was not so specific in her account of her work. She was in a labour camp where the women were called on to do all kinds of work, such as helping to build roads and houses, and for a short time she worked in a silver mine. In July, 1945, Emma was put to work in a tile factory. For the first month she had to lay down boards for the tiles to dry on, but for the next six months she had to clear dust from the chambers in which the tiles were baked. These chambers were very hot and dusty. Afterwards she went back to carrying the boards.

All the women stated that a specific amount of work known as the "norm" had to be done each day. Each group had a different "norm," which was fixed according to the fitness for work, and Ida gave the following example. In her peat-field the "norm" for a Group II worker was to clear eight rows, each 200 paces in length, and this was to be done in eight hours. Group III had only six rows to clear, and this was expected to take six hours. Both groups were therefore thought capable of doing the same amount of work per hour. If the "norm" was not completed within the set time the women had to go on until the rows were finished. If for any reason other than obvious illness the women failed to complete the "norm" they were liable to be given solitary confinement for one to three days. There was no corporal punishment.

All had one free day each week, but some had to do camp cleaning on this day. Although the women longed not to work they did not actually refuse, the reason being perhaps that, as will be shown later, in most cases good work guaranteed better food. All the women said that they were worked to their utmost capacity.

Payment for work was sometimes made in money, sometimes in goods. If, as in Elli's camp, they were paid in money they had to buy all their own food, but the earnings were enough to enable the best workers to buy as much as they wanted. The average worker or sick woman earned less and managed to buy only the food offered in the camp kitchen. In most camps it seems to have been the rule not to pay the women in money but to set the "norm" as the minimum amount of work which guaranteed free food. Extra work—graded in percentage above the "norm"—was rewarded sometimes by money payment and sometimes by material for garments.

### The Food in the Camps

There was general agreement that the food was of very poor quality and inadequate in quantity during 1945 and 1946, but that it improved to some extent later. Despite this improvement all the six women except Elli said that they were always hungry. They usually had three meals a day, but Hanna and Emma had only two. The number and time of Emma's meals were determined by the fact that she had to work for eight hours without a break; meals were served in her camp only at 6 a.m., 12 noon and 6 p.m. The staple items of diet were cabbage soup, bread, and *Brei*, which was a kind of soup made principally from cereal, but Emma received *Brei* only if her work was considered good.

On the average the women seem to have been given 600 to 800 g. of bread per day; the quality of the bread was, however, said to have been very poor. As a rule 0.5 kg. of sugar was issued once a month, but many months

passed without it. Ida said that the younger women often ate the whole pound straight off. She also ate stinging nettles which she had gathered on her way to work. They were eaten raw after she had rubbed them in her hands so that they might not sting her tongue. All the women agreed that the food was not adequate for the work they were expected to do. The meals never satisfied them, and Hanna said that she thought no one could have survived on the basic camp rations. In her camp extra food could be bought. In 1946 she sold her coat for 520 roubles to a Russian civilian and used the money to buy potatoes and some fruit. She said they were always looking through their belongings to see what they could turn into food.

In Margret's camp extra food also had to be bought, but only the men who were fellow prisoners were paid. The women were able to get some of the men's money by doing various jobs for them. Emma in the last two months was able to earn 930 g. of bread a day because, although she was in Group III, her output of work was that expected of a woman in Group II. This was her only way of getting extra food. Agnes could not get food for extra work, but managed to do some needlework and knitting for Russian civilians, who gave her potatoes and milk in exchange. Elli had a different story because her earnings were from 30 to 50 roubles a day and her basic food requirements only cost about half this amount. Bread cost her 3 roubles and 50 kopeks for 1 kg., and a small portion of *Brei* 80-90 kopeks. She was in the comparatively fortunate position of being able to supplement her diet out of her income with such extras as milk, but that cost 10 roubles for 0.5 litre. Meat at 80 roubles for 0.5 kg. was too expensive for her to buy.

The women were asked if they craved for any particular food. Elli said that she had no cravings, as she could have bought anything if she had wanted to pay for it. Ida longed for potatoes and meat—something "*kräftig*"; Hanna for potatoes and something sweet. Emma wanted milk and butter, Margret and Agnes wanted "proper" whole potatoes, *Brötchen mit Wurst*, and cake.

### Living Conditions, Medical Care, and Illness

The permanent camps consisted of a collection of one to four wooden huts set in a compound and surrounded by a wire fence. In the larger camps the compound was about the size of a football ground. There was only one entrance to the camp, which was guarded. The number of women in each camp varied widely, from 80 in Hanna's camp to 1,000 in Emma's. In each camp there were usually a small number of German men who were civilian internees and who had been taken from their homes at the same time as the women. Twenty to thirty women occupied one room, spending their free time there during the day and sleeping there in beds which consisted of double-tiered wooden frames with straw mattresses. All the six women except Agnes had blankets, but she had to use her coat instead. Ida and Emma complained about the bugs, which disturbed their sleep. There was no possibility of any kind of privacy in the camp. Although washing facilities were more or less primitive, and soap was scarce, all the women agreed that they could maintain a reasonable standard of cleanliness. Emma, Margret, and Ida said that they were examined for lice once a week but that hair was shaved only if lice were actually found.

All but Agnes said there was a monthly sick parade, which was held by a German or Russian doctor. It was merely an inspection with the object of reclassification if necessary. In most camps a doctor was available to see acute cases and to decide if an illness was severe enough to prevent the woman from working. Elli said that to be certified as sick there must be fever over 37.5° C., furunculosis, or a swollen face. In Ida's camp there were once considered to be too many women with temperatures over 37.5° C., and so the critical temperature was raised to 37.8° C.

In all except the smallest camps a room was set apart for women who were ill, and they were looked after by a nurse—usually a German girl, who did this instead of other work. This room was only for women who were really ill and was not available for those who merely needed rest. Severe cases were sent to the local civilian hospital or to the hospital of a neighbouring camp centre. Ida unfortunately had diphtheria in her first year. She was sent to the local Russian civilian hospital and was treated like the other Russian patients. She stayed there for four weeks, and was then sent back to camp, where she had to start work again immediately, although she complained of pains and stiffness in her legs, of water running out of her nose when she drank, and of difficulty with her speech. After five days' work she was seen by the Russian doctor, who put her on light work in the camp kitchen for three months. Her condition got worse and worse, and eventually she was sent back to the civilian hospital. There she rested for four weeks, and was then given some kind of light therapy, and her condition began to improve. The most common illnesses seen in the camps were typhoid and diarrhoea, malaria, and furunculosis. Tuberculosis and other lung diseases do not seem to have been especially prevalent. The six women attributed most of the illness to bad food, but Agnes said that much of the illness in her camp was due to the work with lime.

Nearly all the deaths of which the women had any knowledge occurred within the first year, and were attributed chiefly to the bad conditions. Even so, Elli thought that the women who died were those who let themselves go too much, who were very depressed and did not put up a fight. Some women who were beyond caring drank stagnant or polluted water and became ill and died. Some women actually went mad. Hanna told a gruesome story of the first months of her imprisonment, when food was very scanty and large numbers died. She thought that, in proportion to the total numbers, more men died than women. During these first months the whole camp was practically a hospital. Fatigue parties took out the corpses at night to bury them in mass graves. Wolves came and dug up the corpses and ate them, and Hanna was with a party which was sent out to rebury the bodies. Her uncle was one of those who died in her camp.

The six women were asked what illnesses they themselves had suffered from. Margret, Agnes, Hanna, and Emma all had oedema of the legs in varying degrees. Margret had it when she arrived in Russia, and said she noticed it more often on her days of rest than on working days. Her hands and face were also swollen. She and Agnes also had polyuria. As previously mentioned, Ida had diphtheria, and Elli and Hanna had malaria. Ida eventually owed her release to a periodontal cyst which increased steadily in size. The Russian doctors preferred to send her home rather than operate on her. Hanna had typhoid and what she believed to be nephritis. She, Ida, and Margret all had lice, but none of them had typhus. Among minor ailments which were not referred to as illness were very painful pins-and-needles in Elli's hands, Margret's breathlessness, palpitations, and hot flushes, and Agnes's giddiness. Elli, who had started to develop a goitre when she was 16, found that it almost disappeared when she was in Russia. It seemed to enlarge as her general condition improved.

Unfortunately only Elli was able to keep any record of her weight. She weighed 51.5 kg. in 1944, and only 41 kg. in 1947. She weighed 51 kg. on her return in 1948. Hanna, who in 1947 was able to weigh herself on the potato scales, thought that by then she had lost about 23 kg. from her 63 kg. in 1944. Ida thought that she was at one time about 7 kg. under her normal weight, and Margret and Emma merely said that they got very thin.

Lack of clothing was not blamed as a cause of illness. All six women were allowed to keep what clothing they had of their own, and in addition to this were given padded clothing for the winter. The materials they earned by extra work, and other materials and wool which were obtained by barter or purchase, were made up during leisure hours, and it was evident that a great deal of care and trouble were expended on the making of the garments. The women brought back with them to Germany underclothing, blouses, and cardigans, all of which were very well made and proved the interest that was taken in the work. In the early days before needles and other sewing materials were available the men in one camp made knitting-needles from pieces of wire. Skill in needlework was made to serve a double purpose, as some Russian civilians were willing to pay with food for knitting or sewing.

The walk to work and the work itself precluded any idea of physical activity in leisure hours. The women were usually confined to the barrack precincts, but in the last year or so some degree of freedom was allowed. Elli, Ida, and Margret could then go to the nearby village alone, and Agnes was allowed to go into the woods sometimes to gather mushrooms and berries on her free day. In Ida's camp there was dancing once a week to music played on home-made instruments, and in Emma's camp there was even a club with a wireless set and occasionally a film show. There was a reading-room in this club and German newspapers. Agnes said that there were no books in her camp; Margret said books were to be had, but she was not interested in them. The reaction of the six women to imprisonment varied according to their temperament, and most of them appeared to have accepted their fate in a way which, when they were questioned, was expressed by a shrug of the shoulders accompanied by some remark such as: "We had to be contented"; "We did not worry much—it was no use"; or "*Was sollten wir machen?*"

The girls in Elli's camp were perhaps less apathetic. They were living under more normal conditions, because they were paid for their work, and although they had to pay for their own food they could improve their conditions by other purchases. This enabled them to maintain an interest in life, although, as Elli said, they had almost given up hope of ever returning home. They had ceased to worry about it, and disbelieved the rumours of repatriation. Hanna said she always thought, "I must get home," but she tried to be cheerful and to keep in good spirits because she realized that this gave her the best chance of survival. Agnes knew of one woman, aged 35, who tried to escape from Russia and reached Moscow before she was caught. She was said to have been sent to Siberia for fifteen years. The other women knew of no attempts at escape made by women, and laughed at the idea. In some camps a few children had been born, and Ida said that she liked to play with them in her leisure hours. None of the other women seems to have found any outlet for her maternal feelings, but no comment was made which indicated any appreciation of this lack.

The first chance of communication with relations came early in 1946, when most of the women were able to send postcards. Elli said that even the privilege of sending the first postcard was held out as an inducement for the best work. Ida and Elli were the first of the six to receive news from home, which they did in June and September, 1947, but Emma did not hear from her husband until March, 1948. Hanna had no news at all until she reached the British zone; the three other women had postcards from relations in the first three months of 1948. Margret and Agnes both said that not knowing what had happened to their families was almost the worst of their trials. Incidentally, Ida felt that the lack of freedom was the hardest to bear—even worse than the bad food, which was the chief complaint of the other women.

### Menstruation and Sexual Feelings

Before their captivity all the women had menstruated regularly at intervals of 25–31 days, and the periods were normal. They all stopped menstruating in Russia, and their accounts are summarized in the accompanying Table. Only

*Table Summarizing the Menstrual History*

| Name | Age of Menarche | Age when Taken Prisoner | Date of Last Period | Circumstances of Last Period | Date and Circumstances of Reappearance of Menstruation | Comments |
|---|---|---|---|---|---|---|
| Ida .. .. | 17 | 18 | April, 1945 | *En route* to railway base | August, 1948, in Germany | No periods while she was in Russia, but a heavy yellowish discharge every 4 weeks. Headaches and "hot feelings" in the head at the same time as the discharge. She thought other girls had similar symptoms |
| Elli .. .. | 14 | 18 | April, 1945 | *En route* to Russia in railway truck | January, 1946, while working on a collective farm. Periods regular for 3 months, then stopped when she began mine work and did not restart until 1947. Stopped again May, 1948, and restarted August, 1948, in Germany | The restart in 1947 was due, she thought, to better food she received at that time |
| Hanna .. | 14 | 21 | September, 1945 | In hospital for typhoid and malaria | Not yet restarted | She was certain that cessation was due to bad food, as girls who worked in the kitchen menstruated as long as they were getting better and extra food. She herself menstruated "as long as she had any calories in her body" |
| Margret .. | 15 | 23 | January, 1945 | At home | Not yet restarted | |
| Agnes .. | 15 | 29 | April, 1945 | *En route* in railway truck | Not yet restarted | Had headaches and backaches every four weeks |
| Emma .. | 16 | 34 | March, 1945 | While working for Russians (minding horses) before being taken prisoner | Not yet restarted | |

Ida and Agnes noticed anything which might have replaced or formed a part of the normal menstrual cycle.

The women were asked if they were worried by the stoppage of periods. Hanna said that she was worried, but that the doctors reassured her. Margret, Agnes, and Emma were not anxious about it, and Emma thought it was "*sehr praktisch*." Hanna and Elli thought that normal sexual desires persisted, and Elli's replies suggested that if she had found a suitable partner she might have had intercourse with him. She was the only one of the four unmarried women who admitted that she was not a virgin before captivity in Russia. Ida was on very good terms during the last year in camp with a German boy aged 18, but the friendship was of an adolescent type and did not advance to sexual intercourse.

Since their return to Germany the two married women had met their husbands and had opportunities for intercourse. Agnes, who had had a number of years of married life before the war, said that, although she was happy to be with her husband again, she was "*zu schwach*" for sexual relations. Emma, who was married (at the age of 33) while her husband was on leave from the Army and had spent only one other short leave with him, said that her relations with him after their four years of being apart were perfectly normal. Margret dismissed the subject by saying that she was too young and that she was not interested in the men in the camps.

Four of the women knew personally women in their camps who became pregnant while they were in captivity, some of the fathers being German prisoners and others Russians of German or other descent. No details of the menstrual history of the women who became pregnant could be obtained. The children were born in the local hospitals, and all the mothers were able to breast-feed their children. Pregnant women received extra food from the sixth month and during lactation, and Elli said the children in her camp looked very bonny. These pregnancies were not the results of rape. All the women agreed that the danger of rape was over as soon as they were "*verladen*" into their cattle-trucks. (The word *verladen*, which was always used by the women when talking about their train journey, is normally never used for human beings but only for cattle and goods.) All the women except Margret were able to avoid rape during the critical first weeks, and regarded this as very good fortune. Margret said she had been raped "only twice"; she did not enlarge on this statement.

### The Release from Captivity

During the last year there were rumours in most of the camps that release might be near for women in Group III. Previously only women who were unfit for work had been sent home. Release, when it actually came in July, 1948, was sudden and unexpected. Margret, Agnes, Emma, and Hanna were released because they were in Group III, and Hanna said that she was lucky in that the choice was made according to the classification of March, 1948. She had actually since then considerably improved in health. Elli was released because she had had an accident in her mine at Christmas, 1947. She had broken her collar-bone and two ribs when she was crushed between two trucks. Since then she had been on lighter work and made a good recovery. Ida, who was a Group I worker in the last two years, was sent home because of her dental cyst.

All the women gave a similar account of their return journey. Although they again travelled in cattle-trucks until they reached the border of the Russian zone at Frankfort-on-Oder, the conditions were very much better than on the outward journey, and there were no complaints of ill-treatment. They went from Frankfort-on-Oder to Göttingen, where they were medically examined. The very great majority of all the women repatriated at this time were dismissed from hospital care or left hospital at Göttingen of their own accord to join relations in the western zones. Twenty-four women who preferred to stay under medical care after meeting their relations were sent to another hospital at the beginning of August, 1948, and the six women questioned belonged to this party.

Finally all the six women were asked what their plans were for the future. Margret hoped that when she was fully recovered she would be able to join her mother, who had come to the British zone and was trying to build up a home again in Hilden, near Düsseldorf. Ida expected to join her mother, now in a village near Krefeld, and had made inquiries about work in a factory where her brother was working. Hanna planned to keep house for her uncle and cousin in the British zone. Elli's family was widely scattered, and she could not decide what she would do. Her mother was still in her old home in Pomerania, and her father, who had been a prisoner of war in England, was working for a farmer in the Ruhr Valley. She had other relations near Münster and she might go to them. The two married women, Agnes and Emma, intended to join their husbands, who were trying to establish themselves in the British zone. They would leave hospital as soon as they felt completely well.


### Summary

An account is given of the experiences of six German women who were taken into captivity in Russia. This account was compiled from the information they gave after they had returned to Germany. Great hardships were endured at first, but conditions gradually improved, and the women were in good clinical state on their return.

Menstruation ceased soon after the women were captured, and five of them had amenorrhoea for nearly three years.


## P.T.A.P.: THE PRESENT POSITION


BY

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In the prophylaxis of diphtheria A.P.T. has certain drawbacks: it is not constant in its composition and, especially in adults, there may be unpleasant reactions. One of us (L.B.H.), working in the Wright-Fleming Institute of Microbiology, produced a purified diphtheria toxoid which instead of being precipitated by alum was adsorbed on to pure aluminium phosphate—a more suitable compound. To this prophylactic he gave the name P.T.A.P. (signifying *Purified Toxoid* precipitated by *Aluminium Phosphate*).

In November, 1944, it was decided that the results obtained in guinea-pigs with this new diphtheria prophylactic justified field trials (Holt, 1947). At that time we appreciated that numerous important problems arose in diphtheria prophylaxis regarding which there was very little accurate knowledge. These included: (*a*) the route of choice for inoculations—subcutaneous or intramuscular; (*b*) the dose of toxoid (Lf units) administered as adsorbed toxoid for the satisfactory mass immunization of children; and (*c*) the optimal amount of mineral carrier ($AlPO_4$) to employ. The new method gave us complete control of the composition of the prophylactic and therefore promised

that these questions could be answered with a measure of reliability not previously obtainable.

In the preliminary trials very small amounts of aluminium phosphate carrier were employed. The results of these trials (Bousfield, 1947a) revealed two important facts: (1) that aluminium phosphate is an extremely suitable vehicle for adsorbing toxoid when used for human prophylaxis, in that local or general *reactions* were absent or at most trifling; and (2) that the efficiency of the prophylactic, as judged by the Schick conversion rate (S.C.R.) in young children following *one* inoculation, increased as the amount of phosphate was increased, but without clear-cut evidence of an optimal amount. The amounts of carrier eventually used, and with no untoward reactions, were very much greater than would be considered safe if presented as A.P.T.

As the work progressed it was found that samples of P.T.A.P. having a mineral content of 10–15 mg. $AlPO_4$ per ml. gave the best Schick conversion rates (dose 0.5 ml.); that this new prophylactic improved in antigenicity on storage (three months) at room temperature (Bousfield, 1947b); and that consecutive batches, chemically almost identical and of the same age, were antigenically the same (Bousfield, Duke, *et al.*, 1948).

We propose here to set forth further details showing the superiority of P.T.A.P. over A.P.T. in the immunizing of children and some further details about its constitution and use.

## Uniformity of Antigenicity in Successive Batches of P.T.A.P. and A.P.T.

It has been found that successive batches of A.P.T. sometimes show disturbing variations in efficiency when tested in the field (Bousfield, 1947c).

These variations were greatly reduced by the acceptance in 1942 of more stringent provisional regulations (*B.M.J.*, 1942). Even so, although the new regulations eliminated the grossly inferior products they did not solve the problem of variations in antigenicity. These, of course, are more readily demonstrated when the responses to *single* inoculations are observed (Bousfield, 1947a).

Evidence showing the degree of antigenic uniformity obtainable with P.T.A.P. has already been published (Bousfield, Duke, *et al.*, 1948), but it may be useful at this stage to recapitulate. In Table I a summary of the results already published is given together with those obtained recently from single inoculations employing six unselected batches of Government issue A.P.T. It will be noted that with P.T.A.P. the Schick conversion rate varied from 94.1 to 100%, with an average of 96.6; and the rate for A.P.T. varied from 83.5 to 97.5, with an average of 87.5%. These latter figures were obtained with a dose of 0.5 ml., which is two and a half times the officially recommended first dose.

The differences among the samples of each group are not statistically significant in either case, but the difference between the results obtained with P.T.A.P. and A.P.T. is significant.

TABLE I.—*Uniformity, and Performance of Six Consecutive Batches of P.T.A.P.* (30 Lf and 10 mg. $AlPO_4$/ml.), and of Government Issue A.P.T. (Lf>50/ml.) Dosage 0.5 ml.†, Administered Intramuscularly. Children all Schick-positive before Immunization, and Post-Schick-tested Four Weeks After a Single Inoculation.*

| Batch No. | Post-Schick Results | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | P.T.A.P. | | | | A.P.T. | | | |
| | (+) | (−) | Total | S.C.R. % | (+) | (−) | Total | S.C.R. % |
| 1 | 9 | 143 | 152 | 94·1 | 11 | 66 | 77 | 85·7 |
| 2 | 5 | 144 | 149 | 96·6 | 11 | 87 | 98 | 88·8 |
| 3 | 6 | 149 | 155 | 96·1 | 6 | 35 | 41 | 85·4 |
| 4 | 4 | 146 | 150 | 97·3 | 22 | 111 | 133 | 83·5 |
| 5 | 4 | 160 | 164 | 97·6 | 1 | 28 | 29 | 96·6 |
| 6 | 0 | 141 | 141 | 100·0 | 1 | 39 | 40 | 97·5 |
| Total | 28 | 883 | 911 | 96·6 | 52 | 366 | 418 | 87·5 |

* Redrawn from Bousfield *et al.*, 1948.
† Two and one-half times the officially recommended first dose for A.P.T.

*Statistical Analysis of the Results*

| | $\chi^2$ | df | P |
|---|---|---|---|
| P.T.A.P. | 9·284 | 5 | ~0·10 |
| A.P.T. | 8·930 | 5 | >0·10 |
| Comparison | 44·436 | 1 | <0·001 |

Namely, there is no significant heterogeneity between the six batches in either group, but P.T.A.P. is definitely superior to A.P.T.

## Route of Choice

It was thought of some importance to determine whether the immunity response after intramuscular injection differed from that after subcutaneous injection. To answer this question the following evidence may be taken into account: direct observations (Schick conversion rates) made at a fixed time interval on a number of subjects who had been inoculated by one or the other route; the immunity response curves over a period of time following injections by either route; and a combination of the results obtained from the above two methods.

In regard to the first method, samples of P.T.A.P. were employed containing a fixed amount of toxoid (5 Lf in 0.5 ml.) and widely different amounts of aluminium phosphate carrier. The conversion rates were determined 28 days after inoculation. The results, which are summarized in Table II and have their probit analysis depicted in the diagram, show that the intramuscular route gives a significantly better response.

TABLE II.—*Comparative Antigenicity of P.T.A.P. of Varying $AlPO_4$ Content, when Administered Either Subcutaneously or Intramuscularly. (Toxoid Dose Constant at 5 Lf in 0.5 ml. S.C.R. Determined 28 Days After One Inoculation).*

| Mg. $AlPO_4$ Injected | Schick Conversion Rate % | |
|---|---|---|
| | Subcutaneous Route | Intramuscular Route |
| 1·5 | 65·6 (93 cases) | 87·3 (79 cases) |
| 2·5 | 83·3 (54 „ ) | 95·2 (83 „ ) |
| 3·5 | 85·0 (100 „ ) | 92·7 (82 „ ) |
| 4·5 | — | 94·1 (85 „ ) |
| 5·0 | 93·3 (45 „ ) | — |
| 5·5 | — | 92·9 (55 „ ) |
| 6·5 | — | 96·4 (84 „ ) |
| 7·5 | 91·5 (47 „ ) | 97·4 (88 „ ) |
| | (339 cases) | (556 cases) |

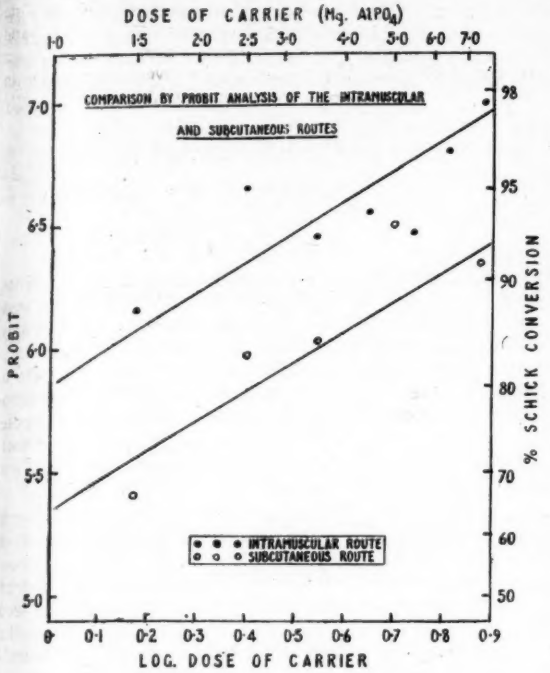
*Statistical analysis of Comparable Groups*

| Mg. $AlPO_4$ Injected | $\chi^2$ | df | P | |
|---|---|---|---|---|
| 1·5 | 10·949 | 1 | <0·001 | |
| 2·5 | 5·346 | 1 | <0·05 | |
| 3·5 | 2·605 | 1 | <0·20 | >0·1 |
| 7·5 | 2·807 | 1 | <0·1 | >0·05 |
| Total | 21·707 | 4 | <0·001 | |

Regarding the second method, no data are available concerning the time for maximal Schick conversion rates in children who had received subcutaneous inoculations of either A.P.T. or P.T.A.P. It has been found in guinea-pigs, however, that when A.P.T. or P.T.A.P. is administered *subcutaneously* the time for maximum antitoxin response was always the same *regardless of the amount of mineral carrier employed*—namely, 25 to 28 days (Holt, unpublished observations). This was correlated with the time for fibrous encapsulation of the residual mass (nodule formation) to occur—namely, some 7 to 10 days.

Since the time interval for the (sterile) foreign-body reaction in the human is the same or even a little less, it seems justifiable on this point to transfer the evidence direct from the guinea-pig to the child.

When an inoculation is made intramuscularly it would seem reasonable to infer that the continuous movement of the muscle fibres would not only usefully disperse the injected particles but delay or even prevent fibrous


DOSE OF CARRIER (Mg. AlPO4)
1·0 1·5 2·0 2·5 3·0 4·0 5·0 6·0 7·0
COMPARISON BY PROBIT ANALYSIS OF THE INTRAMUSCULAR AND SUBCUTANEOUS ROUTES
PROBIT
% SCHICK CONVERSION
7·0 6·5 6·0 5·5 5·0
98 95 90 80 70 60 50
• • • INTRAMUSCULAR ROUTE
o o o SUBCUTANEOUS ROUTE
0 0·1 0·2 0·3 0·4 0·5 0·6 0·7 0·8 0·9
LOG. DOSE OF CARRIER

*Probit Analysis of the Two Curves*

| | $\chi^2$ | df | P |
|---|---|---|---|
| Homogeneity of subcutaneous series .. | 1.620 | 3 | >0.50 |
| Homogeneity of intramuscular series .. | 2.532 | 5 | >0.70 |
| Parallelism between the two curves .. | 1.724 | 1 | >0.10 |

Namely, no significant deviation from parallelism.

Both the subcutaneous route and the intramuscular route show a linear dependence on the probit of the response (percentage of Schick negatives) with the logarithm of the dose of carrier, a result analogous to that shown by Carlinfanti (1948). The two lines are parallel, and the ratio of potency of the intramuscular to the subcutaneous route is 2.6 with 95% fiducial limits of 1.4 and 5.0; therefore the intramuscular route is definitely superior to the subcutaneous route.

encapsulation. Should this occur the antitoxin response curve to moderately large or large doses of P.T.A.P. or A.P.T. should show a peak value later than 28 days after injection. This was in fact found to be the case.

Three sets of figures are available on this point. The Schick conversion rates after a period of time were observed in children who had received *intramuscular* inoculations of 0.1 ml. A.P.T. (Lf 50), 0.5 ml. P.T.A.P (Lf 200, 5 mg. $AlPO_4$/ml.), and 0.5 ml. P.T.A.P. (Lf 190, 8 mg. $AlPO_4$/ml.). In the case of the very small dose of A.P.T. the conversion rate showed a peak value at the sixth week, and in both cases of P.T.A.P.—where much more carrier was employed—the Schick conversion rate was still rising at the end of twelve weeks (Bousfield, 1947c). These observations show that conversion rates obtained *four* weeks after an intramuscular injection of P.T.A.P. would have been higher had the tests been carried out at a later date.

This conclusion, now referred back to Table II, means that in the case of the subcutaneous route the conversion rates found represent maximal ones and those for the intramuscular route submaximal.

From all these considerations it is concluded that the intramuscular inoculation of P.T.A.P. containing reasonably large amounts of mineral carrier results in a more complete utilization of the prophylactic than that following subcutaneous inoculation, with its early fibrous encapsulation of much of the material injected.

## Optimal Amount of Mineral Carrier

In determining the optimal amount of mineral carrier to employ in young children it is not possible to substitute any animal for the child, and it would be unwise in our present state of knowledge to rely too much on investigations based on a weight-for-weight basis between animal and child. The results already published (Bousfield, 1947a) clearly demonstrate the great part played by the amount of carrier inoculated, and reveal that the best conversion rates are obtained with samples of P.T.A.P. containing 10–15 mg. $AlPO_4$ per ml. (see Table II). But to be able to say definitely that 15 mg. is better than 10 mg., or vice versa, involves two serious difficulties, as the percentage differences involved are very small. These difficulties are: (*a*) the rapidly increasing dose of antigen required to immunize the residual less responsive members of a population, and (*b*) because of this, the necessity for studying really large numbers of cases, if it is sought statistically to substantiate any conclusion drawn, when Schick conversion values greater than 90% are achieved.

With the limitations indicated above borne in mind, the evidence shown in Table VI strongly indicates but does not conclusively prove that P.T.A.P. containing 10 mg. $AlPO_4$ per ml. is better than an antigen containing 15 mg.

## Essential Lf Dosage

In order to answer this problem it was considered necessary to use a rather longer time interval between inoculation and the post-Schick test. It was therefore decided to determine the Schick conversion rate three months after a single intramuscular inoculation of samples of P.T.A.P. each containing 15 mg. $AlPO_4$/ml. and different amounts of purified toxoid. The figures obtained from a preliminary test were as shown in Table III.

TABLE III.—*Schick Results*

| Toxoid Injected (Lf) | Three Months After One Intramuscular Injection of 0·5 ml. | | |
|---|---|---|---|
| | (−) | (+) | S.C.R. (%) |
| 5 | 114 | 6 | 95 |
| 10 | 123 | 2 | 98·4 |
| 15 | 118 | 5 | 96 |
| 20 | 124 | 1 | 99·2 |
| 30 | 120 | 4 | 96·77 |
| Total .. .. | 599 | 18 | 97 |

$\chi^2$ (5 Lf/the rest) = 1·8, P = 0·2.

These results do not show any statistically significant differences.

This experiment was repeated. For the more recent trials, *two* similar series of preparations were used, and observations were made at *three* time intervals—three, six, and fifteen months after injection.

It is clear from the results shown in Table IV that, using a dose of 7.5 mg. of $AlPO_4$, the same excellent responses were obtained with amounts of toxoid varying from 10 to 30 Lf. Even with 5 Lf of toxoid the response was not appreciably lowered.

Amounts of toxoid as low as 10 Lf/ml. gave results equally as good as those obtained from the amounts prescribed by the T.S.A. Regulations (50 Lf/ml.). It seems, therefore, that much of the toxoid demanded by the present regulations is wasted when used in P.T.A.P. This is a matter of no small importance economically when toxoid of the quality described is used.

Another point of importance arising from these findings is the *persistence* of the immunity induced by one dose of P.T.A.P., which suggests that we may in fact be in sight of a single-injection prophylactic against diphtheria.

TABLE IV.—*Schick Conversion Rate after One Inoculation of 7.5 mg. of $AlPO_4$, with Varying Amounts of Purified Toxoid (Children Aged 1 Year at Time of Inoculation)*

| Lf Injected | Schick Failure Rate % — Material E.3061 | | |
|---|---|---|---|
| | After 3 Months | After 6 Months | After 15 Months* |
| 5 | 5·0 (120) | 4·0 (50) | 4·08 (47) |
| 10 | 1·6 (125) | 4·1 (49) | 4·08 (49) |
| 15 | 4·06 (125) | 1·9 (52) | 1·75 (57) |
| 20 | 0·8 (125) | 5·6 (54) | 4·76 (63) |
| 30 | 3·23 (124) | 1·8 (58) | 3·64 (55) |
| | 619 cases S.C.R. 97·08% | 263 cases S.C.R. 96·7% | |
| | Duplicate Material E.3143 | | |
| 5 | 5·3 (75) | | |
| 10 | 2·6 (76) | | |
| 15 | 1·4 (72) | | |
| 20 | 1·3 (77) | | |
| 30 | 5·6 (71) | | |
| | (371 cases, S.C.R. 96·7%) | | |
| | Materials E.3061 and E.3143 Combined | | |
| 5 | 4·8 (125) | | |
| 10 | 3·2 (125) | | |
| 15 | 1·6 (124) | | |
| 20 | 3·05 (131) | | |
| 30 | 3·9 (129) | | |
| | (634 cases, S.C.R. 96·6%) | | |

*Statistical Analysis of Results E.3061 and E.3143 Combined*

| $\chi^2$ | df | P |
|---|---|---|
| 2·142 | 4 | 0·7 |

The results are homogeneous, and no statistical difference exists between the several samples.

* This series, tested 15 months after a single inoculation, is obtained by retesting all the children available who were injected with batch E.3061 and found negative three months later. (Although the antigen in Schick toxin results in a definite second response effect, this is transitory and does not affect the immunity level when the tests are repeated 12 months later. This was shown by the study of a further 239 children, who received the same material and were not post-Schick tested until 12 months after the single inoculation. This group showed an overall conversion rate of 95.4%, which compares with an approximate 93.3% for the group (271 cases) which received the intermediate Schick test.) The findings thus represent the *persistence* rate of immunity in children who responded to a single inoculation. To get a true picture of the situation in such a group of children as is shown in the results of the three-months test in batch E.3061 at a period of 15 months (assuming that those who failed had not received a further inoculation), it is necessary to add the percentage of failures in the original group to the failures found 15 months after inoculation. If this is done one can say that the expectation in the five groups not post-Schick-tested for 15 months would be approximately:

| | |
|---|---|
| 5 Lf still Schick + at 15 months | 9·1% |
| 10 Lf " " + " 15 " | 5·7% |
| 15 Lf " " + " 15 " | 5·8% |
| 20 Lf " " + " 15 " | 5·8% |
| 30 Lf " " + " 15 " | 6·9% |

With the possible exception of the 5 Lf series, these figures would compare reasonably favourably with those obtained 15 months after the present routine two-injection treatment with A.P.T.

## *p*H of P.T.A.P.

It was noted by Dr. W. B. Stott (M.O.H., Cuckfield) and one of us (G.B.) that *during* the injection of P.T.A.P. babies showed some signs of temporary discomfort. It was obviously desirable to rectify this if it could be done without affecting the efficiency of the prophylactic.

That the injection of P.T.A.P. in 0.5-ml. doses did cause some pain was confirmed by inoculating a number of adults. The pain, which was trifling and transient, was suspected to be due to the slight acidity of the prophylactic—*p*H 5–5.2. When the reaction was altered to *p*H 7, or even to *p*H 6, and again tested on adults, it was found that, apart from the needle puncture, the injection was painless. It became necessary, therefore, to determine the stability and efficiency of P.T.A.P. prepared in such a way that the final mixture was so nearly neutral that pain was avoided.

A quantity of P.T.A.P. was prepared containing 30 Lf of purified toxoid and 10 mg. $AlPO_4$ per ml.; one part was adjusted to *p*H 5 as usual and the other to *p*H 6.5. Both samples were then left at room temperature (20–22° C.) for six months and tested for potency by animal assay as follows: They were each diluted 1 in 60 with physiological saline, and 1-ml. quantities were injected subcutaneously into normal guinea-pigs.

The dose, therefore, was 0.5 Lf and 0.16 mg. of mineral carrier. The animals were bled four weeks later and the sera from each group pooled. At the same time they were given a second identical inoculation. Two weeks later they were bled again, and the antitoxin titre of each serum was determined. The results obtained are shown in Table V.

TABLE V.—*Animal Assay of Acid and Nearly Neutral P.T.A.P., Lf 30, 10 mg. $AlPO_4$/ml. (Six Months Matured at Room Temperature)*

| | Group A (P.T.A.P., *p*H 5) | Group B (P.T.A.P., *p*H 6·5) |
|---|---|---|
| | Mean Value 28 days after 1 dose | |
| | 0·2 u./ml. | 1·0 u./ml. |
| | Individual Values 14 days after 2nd dose, u./ml. serum | |
| Pig No. 1 | 2·5 | 10 |
| " 2 | 0·2 | 8 |
| " 3 | 7·0 | 7 |
| " 4 | 1·5 | 1·5 |
| " 5 | 1·0 | 3 |
| " 6 | 4·0 | 1·5 |
| " 7 | 2·2 | 4 |
| " 8 | 0·1 | 2 |
| " 9 | 5 | 8 |
| " 10 | 2 | 3 |
| " 11 | 1·25 | 2·5 |
| " 12 | 2 | — |
| Arithmetic Mean .. | 2·4 | 4·6 |
| Geometric Mean .. | 1·48 | 3·4 |

*Statistical Analysis*

$$t = \frac{\bar{x}}{\sqrt{\frac{s^2 (n_1 + n_2)}{n_1 \cdot n_2}}} = 2.1$$

which, for 21 degrees of freedom, gives a P value of 0·05.

From the figures obtained it seemed probable that the prophylactic at a reaction of *p*H 6.5 was actually a better antigen than that at *p*H 5.

For the purpose of determining by *clinical trial* the relative efficiency of nearly neutral and acid P.T.A.P. *three* preparations were made: (*a*) P.T.A.P., Lf 30, 10 mg. $AlPO_4$/ml., *p*H 6.5; (*b*) P.T.A.P., Lf 30, 15 mg. $AlPO_4$/ml., *p*H 6.5; and (*c*) P.T.A.P., Lf 30, 10 mg. $AlPO_4$/ml., *p*H 5. They were matured for six months at room temperature before use.

As before, Schick-positive children between their first and second birthdays were used. The dose administered was 0.5 ml. intramuscularly, and the Schick conversion rate was observed four weeks later. The "pain factor" was assessed on three grounds—"reaction" to (1) the needle-pain, (2) the actual pressing of the syringe plunger (the inoculation proper), and (3) duration of "reaction" after withdrawal of the needle.

These factors were assessed as carefully as possible and were recorded as +, ++, or +++. The total number of plus signs set down against each preparation was divided by the number of cases observed.

TABLE VI.—*Comparison of P.T.A.P. at pH 5 and pH 6.5 (S.C.R. Observed Four Weeks After a Single Intramuscular Inoculation of 0.5 ml.)*

| Composition of P.T.A.P. | | | Post-Schick Results | | | |
|---|---|---|---|---|---|---|
| Lf/ml. | *p*H | $AlPO_4$/ml. | (+) | (−) | S.C.R. | "Pain-factor" |
| A. 30 | 6·5 | 10 mg. | 2 | 206 | 99·0 | 0·68 |
| B. 30 | 6·5 | 15 mg. | 10 | 181 | 94·8 | 0·65 |
| C. 30 | 5·0 | 10 mg. | 4 | 167 | 97·7 | 1·05 |

*Statistical Analysis*

I. Series A and B (comparison of the 10- and 15-mg. preparations at *p*H 6·5):

$\chi^2 = 4.612$; df = 1; P = <0·05

(after Yates's correction for continuity, difference significant at the 5% level).

II. Series A and C (comparison of the *p*H 5 and *p*H 6·5 preparations):

$\chi^2 = 1.47$; df = 1; P = 0·25.

The results, summarized in Table VI, show that there was a greatly reduced overall "reaction" to the *p*H 6.5

mixtures. Furthermore, they reveal that there was no reduction in potency when such mixtures were used—in fact, the results obtained with the 10 mg./ml. preparation were virtually perfect, and indicated that 10 mg./ml. of aluminium phosphate is optimal.

### Résumé, and Conclusion Arising from Latest Findings

It is now four years since field trials on P.T.A.P. were begun. A number of important points had to be unequivocally established. It has been shown that in order to obtain the best results a far greater amount of carrier must be used than would be considered safe if presented as A.P.T. With these very large amounts of carrier the remarkable conversion rates of 97–99% following a single inoculation have been achieved, and this immunity has been shown to persist in 94% of the children for 15 months or more. Of equal importance is the virtual absence of local or general reactions; and not one child in over 6,000 inoculated developed a sterile abscess.

The work progressed in stages. Up to now the optimal amount of mineral carrier has been determined, the route of choice has been found, an approximation of the requisite quantity of purified toxoid has been made, and most of the discomfort of the earlier preparations has been abolished. Also, as a result of improved laboratory technique, the purity of the toxoid employed as routine procedure has been increased to 2,000 Lf/mg. p. $N_2$ (90% pure toxoid). Toxoid of this purity was used in all the more recent work described above.

On the basis of these findings the composition of P.T.A.P. now prepared is as follows:

| | |
|---|---|
| $AlPO_4$ .. .. .. | 10 mg./ml. |
| Toxoid: | |
| (*a*) amount .. .. | 50 Lf per ml. (*by law*) |
| (*b*) purity .. .. .. | 2,000 Lf/mg. p. $N_2$ |
| NaCl .. .. .. | 0.85% |
| Preservative .. .. .. | 0.01% sodium ethyl mercury thiosalicylate |
| Reaction .. .. .. | *p*H 6–6.5 |

The prophylactic is stored at room temperature for three to six months before issue.

### Summary

Purified toxoid, aluminium phosphate precipitated (P.T.A.P.), is an accurately standardized diphtheria prophylactic, which in its antigenicity, stability, and freedom from reactions has distinct advantages over alum-precipitated toxoid (A.P.T.).

Study of the results obtained from experimental work and field trials shows that: (*a*) The optimal amount of mineral carrier for young children is 5 mg. $AlPO_4$, in a 0.5-ml. dose. (*b*) Intramuscular inoculations confer appreciably better immunity than do subcutaneous. (*c*) P.T.A.P. produces a definitely better Schick conversion rate than does A.P.T. A *single* inoculation of 0.5 ml. P.T.A.P. containing 10 or more Lf units of purified toxoid and 10 mg. $AlPO_4$ per ml. produces in children a Schick conversion rate of >95% one month after injection. At three and six months the S.C.R. is still over 95%, and has not fallen appreciably even after fifteen months. (*d*) P.T.A.P., adjusted to *p*H 6, is an antigen at least as efficient as the earlier more acid (*p*H 5) preparation, and causes less discomfort on inoculation.

The composition of P.T.A.P., as now prepared, is accurately described.

For facilities at various stages of this work we desire to thank Dr. A. Anderson, M.O.H., Heston and Isleworth; Dr. H. W. Barnes, M.O.H., Camberwell; Dr. P. L. T. Bennett, M.O.H., Fulham; Dr. H. D. Chalke, D.M.O., No. 7 London Division; Dr. H. Smith, D.M.O., No. 1 London Division; Dr. A. G. G. Thompson, M.O.H., Lambeth; and Dr. W. H. S. Wallace, D.M.O., No. 8 London Division. Grateful thanks are also due to Dr. L. Cavalli, of the Department of Genetics, Cambridge, for assistance in the statistical analyses.

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# A METHOD OF INCREASING THE LUNG BLOOD SUPPLY IN CYANOTIC CONGENITAL HEART DISEASE

BY

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The purpose of this report is to describe an ancillary method of increasing the pulmonary blood supply in patients suffering from congenital cyanotic heart disease in whom the main defect is inadequate blood flow to the lungs. There are already two methods of increasing this blood supply. An anastomosis has been created between a systemic artery and one of the pulmonary arteries (Blalock, 1947; Potts and Gibson, 1948), and valvulotomy has been successfully practised in patients with valvular stenosis (Brock, 1948; Sellors, 1948).

These procedures have improved many seriously incapacitated children. Enthusiasm has been rekindled in a field in which endeavour had almost ceased, and physicians and surgeons have been brought together at a time when "progress" has often led to divergence of paths.

### Theoretical Considerations

It has been found that anastomosis or valvulotomy may not be practicable or advisable in every case. There are patients in whom the pulmonary arteries may be absent or too small for any form of anastomosis. The Blalock type of operation may be impossible if the aortic arch lies at the base of the neck or if there is unusual aortic branching.

The clinical condition of some patients is so serious before operation that even the most skilled and experienced surgeon may hesitate to embark upon a procedure which may take many hours to complete. Conversely, some congenital cardiac deformities alter function to such a minor degree that it is unreasonable to undertake an operation of great magnitude. Therefore, if a simple operation could be devised which offered hope of amelioration it might serve a purpose in *some cases*.

It occurred to one of us (N.R.B.) that a simple alternative method of improving these patients might be to produce vascular pleural adhesions and so to bring blood into the lungs from the parietes. Attempts to revascularize the heart (by omentopexy and similar procedures) have been disappointing, but there are reasons for believing that success might be achieved if the same principles were applied to the lungs. These reasons are:

(*a*) Some children are born without pulmonary arteries and survive; thus blood from systemic collateral vessels can reach the alveoli.

(*b*) In patients suffering from pulmonary tuberculosis in whom an artificial pneumothorax has been induced and

adhesions cauterized it is common to find blood vessels either in the middle of adhesions or, as isolated strands, spanning the pneumothorax from the parietes to the visceral pleura. These vessels carry blood from the extrapleural tissues to the lung and sometimes are the main blood supply to a diseased area: for instance, if vascular adhesions over a large tuberculous cavity situated near the edge of the lung are divided the peripheral wall of the cavity may slough.

(c) At thoracotomy performed on patients suffering from Fallot's tetralogy collateral vessels coming from the mediastinal, the phrenic, and the internal mammary arteries are often seen entering the hilum of the lung. It is well known that in some of these patients death may follow a thoracotomy when an anastomosis could not be achieved, and this may be due to severance of collateral vessels in the course of dissection.

With these points in mind, thoracotomies were performed upon two patients suffering from Fallot's tetralogy, and the experiences obtained gave clinical support to the proposition. The object was to perform a Blalock's operation, but in neither case could the operation be carried out.

The first patient was a small girl. The right chest was opened in the hope that the right subclavian could be anastomosed to the right pulmonary artery. Dense, diffuse vascular adhesions were found, and it was only after these had been divided that the hilum was reached and a very small pulmonary artery isolated. This artery was not clamped, but about twenty minutes later the child died, and at necropsy it was found that the left pleural cavity was obliterated by adhesions and that the left pulmonary artery was also diminutive. Death probably occurred because an important collateral circulation had been removed on the right side as the pleural adhesions were cut to expose the hilum.

The second patient was also a little girl. The aortic arch was high in the mediastinum, and the innominate artery came off so far towards the left side that it was anatomically impossible to approximate the right subclavian to the pulmonary artery. A good deal of dissection in the mediastinum was carried out before the attempt was abandoned, and in the end the mediastinal pleura was not closed because of oozing from the raw surface which was left. After the operation the parents were informed that nothing beneficial had been achieved or could be done; hence it was surprising to find a few months later that the girl was much improved. Before this operation she could walk only 40 to 50 yards (37–46 metres) before becoming severely dyspnoeic, whereas after operation she could walk a mile (1.6 km.). Since then a further operation has been performed on the left side and adhesions have been deliberately created. She can now walk three miles (4.8 km.), has given up her push-chair, and goes to an ordinary school. (See Case 1, below.)

### Surgical Technique

After these experiences operations were developed expressly to create vascular adhesions, and they have been practised when, for the reasons already described, systemic pulmonary anastomosis or valvulotomy seemed to be impracticable. The ordinary methods of pleurodesis, such as the injection of a small amount of strong silver nitrate into the pleural cavity or insufflation of iodized talc, were not used, because it was felt that more effective blood vessels would be created if the surface of the lung was brought into direct contact with the vessels in the chest wall. For this reason the first cases were treated by opening both pleural cavities—at separate operations—and removing the parietal pleura from the upper mediastinum, from the dome of the pleura, and from the upper half of the chest. Powdered asbestos (0.4 g.) was dusted on to the raw surfaces, the chest was closed, and, after instituting temporary drainage, the lung was completely re-expanded.

At each of these operations a fairly extensive examination of the anatomy of the congenital abnormality was undertaken and the pericardium was often opened, but in spite of this the children sustained the procedures well and there has been no mortality. The parietal pleura has not been stripped off the lower part of the chest and the diaphragm, because it was felt that this might reduce the vital capacity too much. We have found that bilateral excision of the pleura actually reduces the vital capacity by about 200 ml. in children under the age of 10 years.

Another type of operation to improve the circulation to the lungs has also been tried. The great omentum has been brought up into the chest and placed in contact with the left lung. The use of the omentum, although attractive in that it carries a large blood supply and can easily be transposed to the lung, is not without theoretical and practical disadvantages. Experience gained in the management of recent chest wounds has shown that whenever a knuckle of omentum passes through a small hole in the diaphragm a diaphragmatic hernia begins to form and steadily increases in size as more and more omentum is insinuated into the pleural cavity. Hence any method of bringing the omentum straight up through a convenient artificial hole in the diaphragm is certain to be complicated by the development of a diaphragmatic hernia. To overcome this the omentum has first been brought up into the upper part of the rectus sheath so that it lies immediately superficial to the muscle fibres of the transversus abdominis and deep to the rectus abdominis. From this point it has been introduced into the left pleural cavity by creating a tunnel in the tissues behind the costal margin and then spread out and stitched in the fissure between the upper and lower lobes of the left lung. As large a surface of the lung as possible has been brought into contact with the omental vessels. Powdered asbestos has been dusted on to the fissural surfaces of the lung before the omentum has been stitched into place.

### Results

This communication is a preliminary report and is submitted because the surgery of congenital cyanotic heart disease is progressing so rapidly that ideas and experiences gained from a small group of patients may be useful stepping-stones to better surgical treatment.

Assessing results of operation is a matter of difficulty. The majority of "blue children" lead sheltered lives and their activity is restricted to a degree which is not commensurate with their ability. Hence a stay of a few weeks in hospital, where the services of physiotherapists and occupational therapists are available, almost invariably improves the morale of the patient and increases functional ability. The sensitive, uncommunicative child lying in bed with clubbed fingers hidden under the bedclothes soon becomes active, and tries to play games and to sit at table with the others for meals. These factors must be taken into consideration before increased exercise tolerance can be attributed to the beneficial result of any particular operation, but increased exercise tolerance is an important method of assessing any treatment and it is of course the criterion by which the patient and relatives judge improvement.

Estimations of arterial oxygen saturation provide evidence of improvement if the conditions under which the blood is taken remain comparable and the child is not upset by the procedure. Decrease of polycythaemia and oxygen capacity is good evidence of improvement if enough time is allowed for correction of post-operative anaemia.

Probably the most satisfactory objective evidence is obtained by the measurement of oxygen intake as a percentage of ventilation before and after a standard exercise according to the method of Cournand (Baldwin, Cournand, and Richards, 1948) and Bing (Bing *et al.*, 1947). From the results of this test the pulmonary blood-flow response to effort can be inferred.

In the following case histories it will be seen that only some of these tests have been carried out in the majority of the patients.

## Case Histories

*Case 1.*—A girl aged 8 years suffered from the tetralogy of Fallot. She was very cyanosed and unable to walk up more than one flight of 12 stairs. She squatted frequently and the edges of her frock were soiled and torn. The oxygen capacity was 25.9 vols.%. The aortic arch was so high in the mediastinum that no systemic artery could be brought down to the pulmonary artery. At the first operation, in April, 1948, the right hemithorax and superior mediastinum were explored. No collateral vessels were found. Three months later she was able to walk one mile on the flat. In August, 1948, the upper half of the parietal pleura on the left side was removed and 0.4 g. of asbestos insufflated. By December, 1948, she could walk two to three miles (3.2 to 4.8 km.) on the flat, was able to climb 50 stairs without dyspnoea, and had ceased to squat. Her arterial oxygen saturation was then 80% at rest and 45% after walking up and down three flights of stairs. Oxygen capacity was 23.3 vols.%.

*Case 2.*—This patient, a girl aged 16 years, had been to an ordinary school but had to be taken there in an invalid chair. She subsequently worked as a bookbinder. She was able to lead only a sedentary life and could not walk up more than one flight of stairs or dance slowly more than once round a ballroom. She suffered from the tetralogy of Fallot, and before the first operation the resting arterial oxygen saturation was 78%. Oxygen capacity was 28.2 vols.%. It was felt that her disability was not of sufficient degree to warrant a major operation. Consequently in May, 1948, a right thoracotomy was performed. A few apical vascular adhesions were present, which were divided when the upper parietal and mediastinal pleurae were removed, and 0.4 g. of asbestos was insufflated over the exposed area. In October, 1948, the same procedure was carried out on the left side. By January, 1949, she was able to walk about 1½ miles (2.4 km.) on the flat and go up three or four flights of stairs, and had attended a dance "without anyone knowing there was anything wrong with me." Her arterial oxygen saturation was then 88% at rest and 60% after walking up three flights of stairs. Oxygen capacity was 23.4 vols.%.

*Case 3.*—A mentally retarded boy aged 13 years was suffering from pulmonary stenosis and an interventricular septal defect. He was very dyspnoeic after walking 50 yards (46 metres) and when in hospital squatted most of the time. The arterial oxygen saturation was 85% at rest. Oxygen capacity was 20.8 vols.%. Oxygen consumed per litre ventilated was at rest 33.5 ml., after standard exercise 26.7 ml. Carbon dioxide produced per litre ventilated was at rest 26.5 ml., after standard exercise 21 ml. In September, 1948, a right thoracotomy was performed. There were no adhesions and no visible collateral vessels. The upper halves of the parietal and mediastinal pleurae were removed and 0.4 g. of asbestos was insufflated. In November a similar operation was carried out on the left side and in addition an omental graft was brought up to the left lung. By January, 1949, he was able to run up and down six flights of stairs without undue dyspnoea and had entirely given up squatting. Arterial oxygen saturation was then 84.5% at rest and 62.1% after exercise. The oxygen capacity was 21.4 vols.%. Oxygen consumed per litre ventilated was at rest 30 ml., after standard exercise 36 ml. Carbon dioxide produced per litre ventilated was at rest 21.7 ml., after standard exercise 23 ml.

*Case 4.*—A well-developed girl of 12 years who had been blue from birth was proved by angiocardiography to have a common truncus arteriosus and absent pulmonary arteries. She attended an ordinary school and was able to walk about 440 yards (400 metres) slowly on the flat, but was very dyspnoeic after ascending three flights of stairs. The arterial oxygen saturation was 57.5% at rest and 44% after three flights of stairs. Oxygen capacity was 33.3 vols.%. Oxygen consumed per litre ventilated was at rest 18 ml., after standard exercise 14.5 ml. Carbon dioxide produced per litre ventilated was at rest 17.5 ml., after standard exercise 12.5 ml. In November, 1948, a left thoracotomy was performed and the absence of a pulmonary artery on the left side was confirmed. There were a large number of collateral vessels entering the hilum. Pleural adhesions were absent. The omentum was grafted into the interlobar fissure, and the upper half of the parietal pleura was removed, 0.6 g. of asbestos being insufflated over the raw surface. Three months later (i.e., after only one side of the chest had been operated upon) her exercise tolerance had increased by about 50%. The arterial oxygen saturation was then 73% at rest and 46% after three flights of stairs. Oxygen capacity was 25.9 vols.%. Oxygen consumed per litre ventilated was at rest 24.5 ml., after standard exercise 23 ml. Carbon dioxide produced per litre ventilated was at rest 22.7 ml., after standard exercise 18.8 ml.

*Case 5.*—A timid girl aged 10 years was suffering from Fallot's tetralogy and arachnodactyly. Her deformities were so great that she had been almost constantly bedridden. She became dyspnoeic after struggling along a few steps. Arterial oxygen saturation was 42% at rest. Oxygen capacity was 30.1 vols.%. In May, 1948, the right hemithorax was explored. The innominate artery bifurcated at the base of the neck, and an anastomosis using the right subclavian artery would have been very difficult. No adhesions were present, but there was some collateral circulation. A large area of parietal and mediastinal pleura was removed and 0.4 g. of asbestos insufflated. In August, 1948, a similar operation was performed on the left side. After many months in hospital she was educated to walk, and by January, 1949, she was able to walk about 50 yards unaided. Arterial oxygen saturation was 55% at rest. Oxygen capacity was 25.8 vols.%.

*Case 6.*—A mentally retarded boy aged 12 years was suffering from Fallot's tetralogy. He had attended an ordinary school, but since 1945 his activities had been so limited by dyspnoea that his attendances became very infrequent. He squatted a great deal and his maximum slow-walking distance was about 100 yards (92 metres). Oxygen capacity was 29.1 vols.%. In July, 1948, a right thoracotomy was performed. There were few collateral vessels and no pleural adhesions. The right subclavian artery was unsuitable for anastomosis because it came from the aortic arch distal to the left subclavian. The pulmonary arteries were very small. Accordingly the right parietal and mediastinal pleurae were extensively removed and 0.4 g. of asbestos was insufflated. A similar operation on the left side was carried out in September, 1948. When seen in February, 1949, he had ceased to squat and his range of activity had increased so that he could walk up 72 stairs or about 440 yards on the flat without discomfort. Oxygen capacity was 22.1 vols.%. His mother reported that she recently went to collect him at school in his wheel-chair, but he had run several hundred yards and arrived home before her.

## Conclusion

Judged by clinical means, such as improved exercise tolerance, diminution of cyanosis, and less frequent squatting, it is considered that there have been two good results (Cases 1 and 3) and that three patients have shown considerable improvement (Cases 2, 4, and 6). One patient (Case 5), whose condition was complicated by arachnodactyly, has been educated to walk, but her skeletal deformity is so great that improvement is difficult to assess.

Of the four cases of which there are details of resting arterial oxygen saturation before and after operation significant improvement has occurred in three (Cases 2, 4, and 5) and no change in one (Case 3).

In six patients the blood oxygen capacity was measured before and after operation and was significantly decreased in four. One patient (Case 3), although clinically improved, showed no change in arterial oxygen saturation or oxygen

capacity, but his oxygen intake and carbon dioxide production, measured as a percentage of ventilation, changed from markedly abnormal to normal figures.

The results may be improved after a longer follow-up period than three to four months, but it is thought that as preliminary observations they are encouraging enough to warrant further application of the procedure to patients who for various reasons are unsuitable for the types of surgery already devised.

Our thanks are due to Miss M. Young, of the Sherrington School of Physiology, and to Dr. Evan Jones and Dr. M. B. Matthews, of the cardiac department, St. Thomas's Hospital. We would also like to state that Dr. James W. Brown has seen these patients and encouraged us to further trials.

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# THE ASSOCIATION OF MATERNAL OBESITY, LARGE BABIES, AND DIABETES

BY

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The obstetric histories of the majority of diabetic women are characterized by an abnormally high foetal loss rate before the onset of clinical diabetes (Miller, Hurwitz, and Kuder, 1944; Miller, 1945; Henley, 1947; Gilbert and Dunlop, 1949). The foetal loss rate shows a progressive increase during this period, reaching a maximum in the immediately pre-diabetic phase, and is higher among women developing diabetes before the age of 45 than among those in whom the disease has its onset after this age.

Allen (1939), in reviewing the obstetric histories of diabetic women, noted that a high percentage of large babies were born many years before the onset of clinical diabetes. Further, Miller, Hurwitz, and Kuder (1944) report the incidence of babies with birth weights in excess of 11 lb. (5 kg.) to be as follows; non-diabetic women, 0.07%; pre-diabetic women, 3.9%; and diabetic women, 6.4%. Miller (1945, 1946) surveyed the birth weights of 22 babies born to 16 mothers who eventually developed diabetes after the age of 40. All deliveries were carried out in the hospital at which these women later sought treatment for their diabetes. Of the 22 babies three weighed 5 kg. (11 lb.) or more, six weighed 4.5 kg. (9.9 lb.) or more, and 15 weighed 4 kg. (8.8 lb.) or more. The number of babies in each weight group was 200, 27, and 7 times the expected incidence respectively, which led him to conclude that women developing diabetes after the child-bearing age are recruited almost wholly from the 5–7% of mothers giving birth to babies weighing more than 4 kg. (8.8 lb.). The recent publication of Kriss and Futcher (1948) confirms these observations. These workers report that 58% of their diabetic women had at some time prior to the onset of clinical diabetes given birth to at least one baby of 10 lb. (4.53 kg.) or more in weight. The average "latent period" between the birth of the first of such babies and the development of diabetes was 24.2 years.

Large babies were formerly attributed to maternal hyperglycaemia, resulting in the transfer of an excess of glucose to the foetus. Bill and Posey (1944), Bigby and Jones (1945), and Henley (1947), however, report the delivery of large babies in spite of well-controlled diabetes, and this has also been my experience.

White and Hunt (1943) and White (1946) conclude from observations of diabetic pregnancies that the unusually large babies are accounted for by an excess of chorionic gonadotropin.

Allen (1939) observed a relationship between excessive maternal gain in weight during pregnancy and the birth of large babies. Watts (1935) and others, who injected into pregnant rats what was at that time assumed to be anterior pituitary growth hormone, observed an unusual gain in maternal weight and in foetal size; such findings may in some measure explain Allen's observations. The report of Miller (1946) again suggests the importance of the growth hormone in the production of large babies: he drew attention to the similarity of the splanchnomegaly observed in the babies of diabetic mothers to that found in acromegalic patients.

Young has often stressed the relationship between the growth-promoting and the diabetogenic effects of anterior pituitary extracts. Thus in 1941 he reported that puppies treated for long periods with daily injections of diabetogenic pituitary extract failed to exhibit glycosuria as did adult dogs, but rapidly increased in weight. Diabetes did eventually develop, however, in some of the animals after many months' treatment. Further injections of the anterior pituitary extract produced only a diabetogenic effect, the growth-promoting influence having been lost. Lukens (1946) suggests that diabetes does not result from an excess of any one anterior pituitary hormone but from the combined oversecretion of both the growth and the adrenotropic hormones.

It is thus apparent that maternal obesity, an abnormally high foetal loss rate, and an unusually high incidence of large babies may occur many years before the onset of clinical diabetes, and that the investigation of women with such obstetric histories may show that a considerable proportion of them become diabetic in the course of time. Such a group of women form the basis of the present investigation.

## Selection of Patients

Pre-diabetic foetal loss reaches a maximum during the two-year period immediately before the diagnosis of diabetes (Gilbert and Dunlop, 1949). It follows that some of the women who in 1941–3 had abnormal obstetric histories but showed no signs of diabetes might in 1948 have developed this disease.

The obstetric histories of 5,000 women confined in the Simpson Memorial Maternity Pavilion, Edinburgh, between August, 1941, and April, 1943, were therefore examined, and 150 of these were found to have unexplained histories of repeated abortions, miscarriages, intrauterine deaths, neonatal deaths, and babies weighing 10 lb. or more. Mimeographed forms asking for the results of all pregnancies since 1941–3 were sent to these women, but owing to the evanescent nature of Edinburgh's wartime population only 75 replies were received. Thirty-five of these gave histories of one or more normal pregnancies since 1941–3 and were therefore discarded from the investigation. The remaining 40 had either not been pregnant since 1941–3 or had had abnormal pregnancies. Of these it has been possible to examine 21 in hospital, the remaining 19 having declined admission owing to pressing domestic obligations.

The usual glucose-tolerance test was performed on all 21 patients, six of whom showed curves which were typically diabetic—i.e., they had fasting blood-sugar levels of more than 120 mg. per 100 ml. and levels which rose to more than 200 mg., remaining above 120 mg. at the end of two hours.

*Table Comparing Patients with Diabetic Blood-sugar Curves and those with Normal Curves*

| | Diabetic G. T. T. | Non-diabetic G. T. T. |
|---|---|---|
| No. of patients | 6 | 15 |
| Age | 39–46 years; aver. 44·2 years | 28–45 years; aver. 39·3 years |
| Obese | 6 | 8 |
| No. of live births | 25 | 40 |
| No. of babies more than 10 lb. | 11 | 5 |
| No. of patients with babies of 10 lb. or more | 5 | 3 |

G. T. T. = Glucose-tolerance test.

From the accompanying table it will be seen that the average age of those patients with diabetic blood-sugar curves was five years above that of those with normal curves. It seems probable, therefore, that some women of the latter group may yet develop a diabetic tendency.

The very high incidence of obesity is remarkable, 14 of the 21 patients being more than 14 lb. (6.35 kg.) in excess of the normal mean weight for their age and height, while all six patients with diabetic blood-sugar curves were 30 lb. (13.6 kg.) or more above their "correct" weight. All patients dated the onset of obesity from their first or second pregnancy, and with each successive pregnancy there had occurred a further gain in weight. Obesity was a less pronounced feature among the women with normal blood-sugar curves than among those who had become diabetic.

Women with unsatisfactory first pregnancies are usually admitted to the Simpson Memorial Maternity Pavilion for second and subsequent confinements. Consequently, accurate birth weights of the majority of viable infants in this group were available. The difference in the incidence of babies weighing 10 lb. or more among the diabetic and non-diabetic groups of women is striking—11 out of 25 compared with 5 out of 40. Thus there seems to be an association between the production of large babies and ensuing maternal diabetes.

### Obese Non-diabetic Women

The high incidence of obesity among women with unsatisfactory obstetric histories suggests that maternal obesity may be related to a high foetal loss rate. The second step in the present investigation therefore consisted in a survey of the obstetric histories of 84 obese non-diabetic women attending the dietetic out-patient department of the Royal Infirmary, Edinburgh. All patients were interviewed personally. The group was unselected, and represented 84 consecutive attendances of obese non-diabetic women at the department.

As in the previous group of patients, the vast majority of these women associated the onset of obesity with an early pregnancy. The ages of these patients varied between 35 and 72 years, with an average of 46.8. Among the 341 pregnancies involved there was a foetal loss rate of 13.4%. This rate is similar to the pre-diabetic foetal loss rate of 12.5% observed by Gilbert and Dunlop in women developing diabetes after the age of 45, the majority of whom were over weight, and contrasts with the control foetal loss rate of 8%.

The majority of confinements among the obese non-diabetic women and among the women developing diabetes after the age of 45 were carried out either at home or in institutions from which birth-weight records were not available. Consequently it was impossible to ascertain the precise incidence of large babies. However, many patients spontaneously volunteered the information that they had had large babies, quoting birth weights of up to 14 lb.

### Discussion

The present investigation reveals that six out of 21 women who had had obstetric histories of a high foetal loss rate and who had given birth to babies weighing 10 lb. or more eventually developed diabetes and that the diabetes was associated with obesity. Thus the incidence of diabetes in those women far exceeds the expected incidence of diabetes in a similar age group of women which is given by Joslin (1946) as 0.864%. The association between the production of large babies and the development of maternal diabetes which was noted by Miller (1945) and Kriss and Futcher (1948) is therefore confirmed by the present study.

The abnormally high foetal loss rate in the obese non-diabetic women of the present survey is similar to that occurring in the obstetric histories of women developing diabetes after the age of 45, most of whom were also obese (Gilbert and Dunlop, 1949). The unusually high incidence of the birth of large babies was a further similarity in the obstetric histories of these two groups of patients. The present observations therefore suggest that close correlation exists between increasing maternal obesity, the production of large babies, and ensuing maternal diabetes.

Both clinical and experimental studies suggest that the anterior pituitary lobe plays an important part in the production of obesity, large babies, and diabetes. The frequent onset of obesity and diabetes at the time of the menopause has been attributed to anterior pituitary overactivity secondary to the loss of the inhibiting effect of oestrogens on the pituitary. Further, the onset of obesity and a diminished carbohydrate tolerance following spontaneously occurring or artificially produced amenorrhoea, as was reported by Ogilvie (1935), supports this hypothesis. The reported results, however, of oestrogen therapy in menopausal diabetes are conflicting.

Young (1941, 1945), from his experimental observations, concludes that excess diabetogenic activity of the anterior pituitary lobe may be balanced by hyperfunction of the pancreatic islets induced through an overproduction of the anterior pituitary pancreatropic hormone. The effect of such a balance is the production of growth by a reduction in carbohydrate oxidation and an associated conservation of nitrogen (Young, 1941, 1945; Ogilvie, 1944). The resulting growth manifests itself, according to the age of the patient, either in the abnormal height of the pre-diabetic juvenile or in the obesity of the middle-aged subject. This growth is maintained only so long as the pancreatic islets respond to the excessive secretion of pancreatropic hormone, but ultimately islet exhaustion may supervene, manifesting itself in cessation of growth and clinical diabetes. Other observations are in accord with this hypothesis. Thus, Ogilvie (1933, 1935) has reported pancreatic islet hypertrophy in a high proportion of obese non-diabetic subjects and a latent period of many years between the onset of obesity and the occurrence of diabetes. Further, Joslin (1946) notes that a rapid loss of weight by obese subjects may precede the onset of diabetes.

Applied to the present study these findings suggest that the anterior pituitary growth factor may be in part responsible for the maternal obesity and diabetes, and that this factor passes across the placenta, causing the foetus to be both abnormally long and abnormally fat. The foetus

thus appears to combine the type of growth displayed by both the pre-diabetic juvenile and the obese middle-aged diabetic.

The clinical and experimental observations discussed suggest that an excessive secretion of the anterior pituitary growth factor during pregnancy may account for the production of progressive maternal obesity, large babies, and ultimate maternal diabetes.


### Summary

Twenty-one women with obstetric histories of unexplained abortions, miscarriages, intrauterine deaths, stillbirths, and neonatal deaths, and the birth of babies weighing 10 lb. or more, were admitted to hospital for investigation. Six of these patients were found to be diabetic. All six were grossly obese and five had had babies weighing 10 lb. or more.

Evidence is brought forward to show a correlation between progressive maternal obesity, the birth of unusually large babies, and ensuing maternal diabetes. It is suggested that an excessive secretion of the growth factor during pregnancy may account for the associated phenomena.


I wish to thank Professor D. M. Dunlop and Dr. R. F. Ogilvie for their helpful advice and criticism, and Professor R. J. Kellar for so kindly putting the case records of the Simpson Memorial Maternity Pavilion at my disposal.

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# GLOSSITIS IN ADDISONIAN PERNICIOUS ANAEMIA

## EFFECT OF SYNTHETIC VITAMINS OF THE B COMPLEX


BY

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Glossitis has been recognized as a common feature of Addisonian pernicious anaemia since the work of Hunter (1909). Some evidence of involvement of the tongue is obtained in about 70% of cases (Brown, 1946). Adequate treatment of the anaemia with potent liver extract usually results in the disappearance of oral symptoms.

Glossitis is also a common feature of the sprue syndrome and of many deficiency states such as pellagra. Its occurrence has been attributed to deficiency of specific vitamins such as nicotinic acid and riboflavin. The fact that the sore tongue of the pernicious anaemia syndrome is indistinguishable from that occurring in well-recognized nutritional deficiencies suggests that in pernicious anaemia it may again be due to a vitamin deficiency, and that it may be corrected by appropriate treatment with one or more of the members of the vitamin B complex.

The present report describes the occurrence of glossitis and a syndrome suggestive of ariboflavinosis in patients with Addisonian pernicious anaemia and the effect of treatment with certain synthetic vitamins of the B complex.

### Clinical Observations

Seven patients with pernicious anaemia are described in whom there was a well-marked disturbance suggestive of deficiency of one or more members of the vitamin B complex. The diagnosis of pernicious anaemia was made on the following grounds. In all cases the clinical picture was compatible with the diagnosis; all had a macrocytic anaemia with a megaloblastic bone-marrow reaction which showed a satisfactory response after treatment with highly purified liver extract; all had a histamine-fast achlorhydria; and in none was there evidence of steatorrhoea or dietary defect.

Of the seven patients, six had severe painful glossitis. Five of the six had been receiving parenteral liver therapy for periods ranging from four months to two years; they were receiving it regularly every two to four weeks during the period of this present study. As indicated in the case reports, the glossitis had either existed since the original illness or developed during its treatment with parenteral liver. The development of a sore tongue was not always controlled by liver therapy, and on occasion bore no relation to the immediate or subsequent haematological status of the patient. In the seventh case (treated for five years) glossitis was associated with angular stomatitis and vascularization of the cornea.

### Case 1

A man aged 58 developed pernicious anaemia, for which liver therapy was started in February, 1946. His tongue was red, glazed, and smooth, but did not cause pain until June, 1946, when its appearance deteriorated and it became extremely sensitive and painful. Blood levels at this time and during the subsequent six months were maintained above 4,500,000 red cells per c.mm. by regular administration of anahaemin. From June 15, 200 mg. of nicotinic acid daily for seven days left the condition of the tongue, if anything, worse. On June 22 100 mg. of calcium pantothenate was given intramuscularly and then 100 mg. daily by mouth.

By the third day discomfort had disappeared; by the seventh day only slight redness at the tip remained, and by July 6 the organ was merely clean and atrophic. Calcium pantothenate was stopped on July 6, and from this date only routine liver therapy was given. Lingual discomfort returned within 14 days. By July 27 the organ was diffusely red and raw-looking, painful, and extremely sensitive, with numerous deep fissures. From July 27, 100 mg. of calcium pantothenate was given daily by mouth. By the fourth day undue discomfort could not be provoked even by hot foods or by deliberate friction against the teeth. By the seventh day objective evidence had almost entirely disappeared. By Aug. 17 the tongue looked more nearly normal than at any time since the patient had first been seen. Atrophy was less marked and central furring had developed. Fissuring was no longer present. Treatment with pantothenate was discontinued, and by March, 1947, there had been no recurrence of the glossitis.

### Case 2

A married women aged 40 had received liver therapy for two years, when the tongue, previously pale and atrophic, became red and very uncomfortable. When seen with this complaint in February, 1946, blood values had been maintained for two years at normal levels (between 4,800,000 and 5,570,000 red cells per c.mm.). From Feb. 23, in addition to the continued regular administration of highly refined liver extract (anahaemin), 300 mg. of nicotinic acid was given daily by

mouth. Gradual improvement occurred, and by April 13 the only visible abnormality was slight marginal redness. The organ was still uncomfortable and unduly sensitive to hot foods. Continued treatment failed to improve matters, and nicotinic acid was stopped on April 27. She continued to receive regular injections of liver extract (anahaemin), but symptoms gradually returned. By Aug. 24 severe general glossitis was present. From this date she was given 100 mg. of calcium pantothenate daily by mouth. From the fourth day the tongue was comfortable, and by the seventh nothing abnormal was evident except slight atrophy. Treatment was stopped. Symptoms returned at beginning of November, and by the 23rd severe marginal glossitis was present, causing great discomfort. From this date she was given 100 mg. of calcium pantothenate daily by mouth. By the third day the tongue was almost completely asymptomatic. By the seventh day it looked almost normal, and by the 14th day it showed only a smooth atrophic veal-like condition. Treatment was stopped. Up to February, 1947, there had been no return of symptoms.

### Case 3

A man aged 61 had received liver therapy for pernicious anaemia for nine months. His tongue had been normal in appearance and sensitivity during this period. In spite of continued regular treatment, and in the presence of blood values unchanged above 4,300,000 red cells per c.mm., from June, 1946, he gradually developed a painful glossitis. By July 27 the organ was diffusely affected and extremely sensitive and remained so without change until, from Aug. 24, 100 mg. of calcium pantothenate was given daily by mouth. Great subjective improvement was noted within 48 hours, and by the seventh day the organ was not even unduly sensitive. It was also normal in appearance. Calcium pantothenate was stopped, and up to March 15, 1947, there had been no return of symptoms.

### Case 4

A married woman aged 58 had had a sore tongue before liver therapy was begun for pernicious anaemia in 1946, and during maintenance treatment which kept blood levels at above 4,500,000 red cells per c.mm. she suffered almost continuously. On June 7, 1946, after about two years' observation and treatment, the tongue showed a severe marginal glossitis with numerous sharp-edged fissures. It was extremely sensitive. By Aug. 3, in spite of continued treatment with liver extract, conditions remained unchanged. She was given 100 mg. of calcium pantothenate intramuscularly. Within 48 hours all discomfort had disappeared and within seven days signs had almost completely disappeared. Routine liver therapy thereafter failed to maintain this improvement, although the red cell count did not fall below 4,400,000 per c.mm.; but within five weeks of giving pantothenate the tongue had returned to its previous condition. On Oct. 6 a further 100 mg. of calcium pantothenate was given intramuscularly. Within 48 hours marked improvement had occurred, and by the seventh day all evidence of active glossitis had disappeared. Return of symptoms was evident in about three weeks, and by Nov. 2 active glossitis was again fully established. From this date 50 mg. of calcium pantothenate was given daily by mouth. By the third day the tongue was much less sensitive, and by the seventh day all discomfort had disappeared and the organ looked merely pale and atrophic. Treatment was stopped and conditions in the mouth remained unchanged for almost a year. In October, 1947, active glossitis again appeared, uninfluenced by continued regular administration of liver extract and with blood levels above 4,500,000 per c.mm. throughout. By Nov. 10 the tongue showed diffuse redness and was extremely sensitive. A simple dose of 50 mg. of pantothenate was given intramuscularly. Within 48 hours symptomatic relief was evident, and on the seventh day all redness had disappeared, but the tongue was atrophic. There had been no return of symptoms up to May, 1948.

### Case 5

A woman aged 73 was admitted to hospital in April, 1944, on account of pernicious anaemia associated with severe glossitis and stomatitis. The tongue was diffusely red and showed slight fissuring. The oral features were unaffected by liver therapy even when this was given twice weekly (4 ml. of anahaemin on each occasion). The blood count rose with a reticulocyte response in an unusually slow fashion, and throughout the following observation period the red cell levels failed to reach 4,000,000 per c.mm. Administration of 150 mg. of nicotinic acid daily by mouth from May 19, 1945, was followed by great improvement. By the seventh day the tongue was less sensitive and looked much less raw. The lips had healed completely. By the 14th day the tongue was merely atrophic and all discomfort had disappeared. Continuation of treatment for four months failed to improve the atrophy. After about two months' treatment with liver extract alone, active glossitis again became troublesome, and by February, 1946, the tongue had returned to its previous condition. On this occasion repetition of nicotinic acid treatment (150 mg. a day) was beneficial, but failed to relieve the condition completely. Treatment was stopped after three weeks, and 5 mg. of riboflavin was given daily by mouth from Feb. 28. Complete subjective and objective evidence of active glossitis disappeared within seven days. Treatment was stopped, and by June 3 symptoms had returned. On this date 100 mg. of calcium pantothenate was given intramuscularly. During the following 10 days the glossitis gradually became more severe. On Aug. 14 administration of riboflavin was again begun (5 mg. a day), with complete subjective and objective recovery by the seventh day. Further observations on this case were not possible.

### Case 6

A married woman aged 58 was first seen on account of a sore tongue which had been troublesome for about two years. She was found to have pernicious anaemia. The tongue was diffusely red over the dorsum and very sensitive, although sensations of taste were impaired. From April 5, 1947, treatment with liver extract being withheld, 50 mg. of calcium pantothenate was given daily by mouth for seven days; no benefit resulted. After a further seven-day period of observation riboflavin was given in doses of 5 mg. daily for a week, again without benefit. Thereafter nicotinamide in daily doses of 200 mg. for two weeks was associated with slight aggravation of the glossitis. From May 10 folic acid was given by mouth in doses of 20 mg. a day. By the seventh day marked relief had occurred, and by the 10th day it was complete. By the 14th day the tongue was normal in appearance. A satisfactory haematological response also occurred with this treatment, and by Aug. 16 the tongue and the blood levels were normal. Folic acid was discontinued. Within four days the tongue became uncomfortable and active glossitis gradually progressed until liver therapy was begun on Aug. 23. Thereafter both anaemia and glossitis remained adequately controlled.

### Case 7

This woman, aged 61, had been receiving liver therapy for five years, when she failed to receive adequate treatment and relapsed. During recovery from this relapse, with weekly administration of 4 ml. of anahaemin and with a red cell count of 3,410,000 per c.mm., she developed a very severe bilateral angular stomatitis involving the mucocutaneous junction, marginal glossitis, and vascularization of the cornea in the upper and outer quadrants, more pronounced in the left eye, where penetration of small vessels amounted to about 2 mm. There was also severe conjunctivitis. Treatment with riboflavin was begun on Dec. 28, 1946. Within a week the angular stomatitis and the conjunctivitis had improved, and by Jan. 25, 1947, the corneal change was seen to be receding. By Feb. 1 the tongue and lips were normal, and within a further 14 days the eyes also were normal. Riboflavin was discontinued after a short period. There was no return of symptoms.

*Summary of Results of Treatment.*—The results obtained by the administration of synthetic vitamins of the B complex to these patients are summarized in the accompanying table. No single substance was found to be effective throughout all cases, and although consistent results were obtained in the one individual with a single vitamin for periods up to 15 months (Case 4), it was also found in one

*Table Summarizing Results of Treatment*

| Case No. | Sex | Clinical Status | Blood Level (Millions) | Lesions | Effective Treatment | Vitamins Ineffective |
|---|---|---|---|---|---|---|
| 1 | M | Treated 4 months | 4·5 + | Glossitis | Pantothenate, oral + i.m. | Nicotinic acid |
| 2 | F | Treated 2 years | 4·8—5·8 | ,, | Pantothenate, oral | Nicotinic acid (partial effect) |
| 3 | M | Treated 1 year | 4·3 + | ,, | Pantothenate, oral | — |
| 4 | F | Treated 2 years | 4·4 + | ,, | Pantothenate, (1) i.m., (2) oral | — |
| 5 | F | Treated 1 year | 3·5—4·0 | Glossitis, stomatitis | Nicotinic acid, riboflavin | Nicotinic acid later inadequate |
| 6 | F | Untreated | 3·4 | Glossitis | Folic acid | Pantothenate, nicotinamide, riboflavin |
| 7 | F | Treated 5 years | 3·41 + | Glossitis, angular stomatitis, vascularization of cornea | Riboflavin | — |

instance (Case 5) that different vitamins might be effective at different times against apparently similar lesions.

## Discussion

The significance of glossitis in pernicious anaemia is not understood, but it is generally recognized that if sore tongue is a feature before treatment is begun it is usually cured by liver extract. Indeed, so commonly does the glossitis respond to liver extract that it has been said that reappearance of tongue manifestations in patients under treatment is an indication of inadequate therapy (Wintrobe, 1946). This suggests some direct relation between the glossitis and the anaemia. There is, however, evidence to the contrary (Oatway and Middleton, 1932; Brown, 1946).

In the present series glossitis occurred without obvious relation to present or subsequent blood levels (see Cases 1, 2, and 4 especially). The significance of this is not clear, especially in view of the apparent rarity of such an occurrence in the experience of others (Wintrobe, 1946). It seems unlikely from what is known of the individual patients that exceptional dietary inadequacy was by itself responsible. All had good appetites and were taking apparently adequate diets. The possibility of a combination of minor defect of absorption in pernicious anaemia and a sub-optimal post-war dietary cannot be entirely discounted. The question arises whether increased dosage with liver extract would have been effective treatment for the glossitis. No definite answer can be given from these results, which are concerned with the effect of single pure substances, but it should be noted that blood counts were maintained at normal and even high levels (Case 2), and in spite of this the tongue was sore. In addition Case 5 received unusually large doses of liver extract without effect on the tongue.

It would seem possible that the development of a sore tongue in pernicious anaemia reflects a breakdown in a metabolic system similar to that responsible for the megaloblastic marrow and the neurological changes. The fact that in this series the glossitis could be controlled by the administration of synthetic vitamins suggests that the breakdown may involve the availability of the vitamin found effective. Members of the B complex exist in natural foods often in a conjugated and not immediately available form. The suggested breakdown in availability may occur at this stage in assimilation, or later in closer relationship to their final functions as parts of enzyme systems concerned with cellular metabolism. Liver extract contains a factor which in the majority of cases rectifies the defect responsible for the mucosal changes and at the same time corrects those responsible for the marrow and neural disturbances. Vitamin $B_{12}$, which may be identical with the anti-pernicious-anaemia principle of liver, has been found effective against the anaemia, the neurological changes, and the glossitis. Conceivably this substance may promote the utilization of certain other essential substances, some of which are well-known vitamins of the B complex.

The role of pantothenic acid in human nutrition is not yet fully understood, and the instances described here are believed to be the first in which this substance has been found to influence symptoms in pernicious anaemia. If this effect represents restoration of an actual deficiency it is difficult to account for the latter except on the basis of a metabolic disturbance secondary to a more fundamental defect such as that already suggested. Pantothenic acid is widespread in Nature, and a deficiency conditioned in such a way seems more probable than one due simply to inadequate intake, especially in persons whose diet is not obviously abnormal.

## Summary

Seven patients with Addisonian pernicious anaemia are described each of whom had a sore, red, raw-looking tongue. One also had angular stomatitis and vascularization of the corneae.

In each case it was found possible to control these changes with a single member of the vitamin B complex in pure form. Four cases of glossitis responded to calcium pantothenate, and one each to nicotinic acid and folic acid. One case responded first to nicotinic acid and later to riboflavin. The patient with glossitis, angular stomatitis, and vascularization of the corneae responded to riboflavin.

The significance of these findings is discussed, and it is suggested that the epithelial changes described reflect a breakdown in some metabolic system which may be similar to that responsible for the megaloblastic marrow and the neurological complications of pernicious anaemia.

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# UNUSUAL SYMPTOMS IN PETROL-TANK CLEANERS

BY

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On Sept. 18, 1945, men from a certain labour unit were employed in cleaning a large petrol tank. It had just been drained of its contents, and to overcome the effects of undue exposure to the petrol vapour inside the tank the men were ordered to work in frequent shifts. The air inside the tank was not rendered gas-free, nor were the men given any airline masks or special clothing to wear. After the initial respiratory discomfort and irritation of the eyes the workmen became accustomed to the vapour and some of them stayed in longer.

Two men, whose cases are recorded below, went to the extreme and worked almost continuously for nearly seven hours. No adverse effects during this period prevented them from doing so. Towards the end, however, they

were seized with intense giddiness and they staggered and fell. They were rescued in an unconscious state by other workers. With first-aid measures both came round in about half an hour and complained of severe vertigo, a sense of constriction in the chest, and pains all over the body. They had to be carried to their quarters. The course of their illness was as follows.

### Case 1

A man aged 25 was admitted to hospital the day after exposure to petrol vapour. Vertigo was severe and he complained of headache, marked loss of muscular power, soreness of the throat, irritation of the eyes, loss of appetite, and numbness, coldness, and intense pain in the lower limbs; pain in other parts of the body was less acute. Apart from congestion of the throat and eyes there were no abnormal physical signs.

*6th Day.*—The patient was improving. The calf muscles were, however, acutely tender on pressure. The knee- and ankle-jerks were sluggish. Five multivitamin tablets, each containing vitamin $B_1$, 1 mg., vitamin $B_2$, 1 mg., nicotinic acid, 10 mg., and ascorbic acid, 25 mg., were given three times a day.

*10th Day.*—Improvement was marked. Only slight pain remained in the lower limbs. Next day he was discharged as cured at his own request.

*16th Day.*—He returned to the hospital with headache, vertigo, and Parkinsonian tremor of both hands and early rigidity. He was irritable and irrational.

*26th Day.*—Parkinsonian rigidity and tremor were well established, and frequent oculogyric spasms were accompanied by spasms of the muscles of the face and mouth. His face, which was very pale, and his attitude, voluntary movements, and speech, were typical of the disease. Mental and bodily asthenia was profound, and most of the time the patient lay quiet in bed, showing no interest in himself or his surroundings. Rarely he asked for a bed-pan or urinal; mostly he passed his urine and stools in bed. His mood was very changeable, and he often cried without apparent reason. There was progressive loss of weight. The ankle-jerks were very feeble, but the calf muscles were not tender. The knee-jerks were slightly exaggerated and the abdominal reflexes were rather brisk. Heart sounds were very feeble. The pulse was regular, 72 a minute, and of low tension and volume. Blood pressure was 95/70 mm. Hg. Respiration was normal, and the temperature was usually subnormal. Both eyes were slightly icteric (effect of suppressive mepacrine). There was still conjunctivitis of the right eye. Urine showed no albumin, sugar, or abnormal quantities of lead, and deposits were normal. Stools were also normal. A blood count showed: Hb, 120% (Sahli); red cells, 6,830,000 per c.mm.; white cells, 12,600 (polymorphs 68%, lymphocytes 23%, mononuclears 2%, eosinophils 1%, and basophils 6%). There were no malaria parasites in the smear. The bilirubin content of the blood was 0.7 mg. per 100 ml. (icterus index 3.5). Blood urea was 16.6 mg. per 100 ml. Wassermann and Kahn reactions were both negative. The patient weighed 118 lb. (53.52 kg.), having lost 23 lb. (10.43 kg.) since the onset of the disease. He was put on a nutritive high-protein diet of over 4,200 calories. In addition 10 multivitamin tablets were given thrice daily. Suppressive mepacrine was stopped.

*36th Day.*—For the first time during his stay in hospital the patient had a temperature of 100° F. (37.8° C.) at 6 p.m. Blood smears and thick drops were negative for malaria parasites. Subsequently the temperature was 99° F. (37.2° C.) at 10 p.m., 99.6° F. (37.55° C.) at 2 a.m. next morning, and once again normal at 6 a.m. and after. Between 1 and 10 a.m. he passed four samples of characteristic haemoglobinuric urine, the first very dark, the second and third dark brown, and the fourth considerably lighter. Subsequent samples were progressively normal to the naked eye, although spectroscopic examination showed the presence of oxyhaemoglobin till the next morning. Apart from the transient low fever described above there were no constitutional symptoms and no haemoglobinaemia in a blood sample taken at 10 a.m. Haemoglobin fell from 125 to 120%, and the red cells from 6,830,000 to 6,510,000 per c.mm. The leucocytosis was raised from 12,600 to 14,200, with polymorphs 72%, lymphocytes 20%, mononuclears 2%, eosinophils 1%, and basophils 5%. There were no malaria parasites in the smears or thick drop preparations. Spectroscopically, serum collected from blood taken at 10 a.m. with care to prevent haemolysis showed only traces of oxyhaemoglobin, and the icterus index remained at 3.5. There was no appreciable rise in blood urea. The Donath–Landsteiner reaction, the acid-serum test, and the Wassermann and Kahn reactions were negative. Spherocytosis was absent and fragility of red cells was normal. No haemolysins were found *in vitro* in the serum. Urine did not show any evidence of abnormal quantities of lead excretion. Alkalis and fluids were given by mouth, and, on empirical grounds, 20 ml. of concentrated antivenene was injected intramuscularly to prevent further haemolysis.

*48th Day.*—Improvement set in fairly rapidly. Rigidity and tremor were less pronounced. Headache, giddiness, and oculogyric spasms disappeared. His mood was less changeable and he was taking general interest all around. He was able to stand and to walk slowly by himself, and his weight had begun to rise. Insomnia still persisted.

*76th Day.*—The patient was now almost completely normal. A noticeable feature was a fall in his erythraemia; the red cells were now 5,200,000 per c.mm., and the Hb was 90%. The blood pressure was 120/80 mm. Hg. Insomnia was less troublesome. Mentally he was still moody and depressed.

*96th Day.*—He was discharged completely cured.

### Case 2

A man aged 23 was admitted on the day after exposure to petrol vapour. His complaints and condition were essentially similar to those of Case 1, but vertigo was very severe and he had considerable pain associated with pins-and-needles in all parts of the body. The throat was very congested and there was conjunctivitis of the right eye. Unlike Case 1 there was no temporary improvement and the patient was completely bedridden.

*13th Day.*—He developed a Parkinsonian tremor of both hands, at first only when he attempted a voluntary movement, but two days later at rest also, with early rigidity. He was becoming very irrational.

*26th Day.*—His complaints were identical with those of Case 1, but he was more severely affected. Most of the time he was depressed and cried without any obvious reason. He talked of his family in trouble, which he said would finish without his help. Later he started getting out of bed and running away, and often fell and injured himself. He complained of the sisters and nursing orderlies harassing him, the loss of his pay-book although it was still with him, and a sense of impending death. He said he was guilty, and persistently begged for pardon for all the sins he had committed. There were physical signs of bronchitis at both bases. Heart sounds were very weak. The pulse was regular, 80 a minute, of low tension and volume. The blood pressure was 110/80 mm. Hg. Respiration was normal and the temperature was usually subnormal. Stools were strongly positive for ankylostoma ova. The urine contained no albumin, sugar, or abnormal quantities of lead, and deposits were normal. A blood count showed: Hb, 80%; red cells, 5,630,000 per c.mm.; white cells, 6,800 per c.mm. (polymorphs 62%, lymphocytes 26%, monocytes 4%, eosinophils 0%, and basophils 8%). There were no malaria parasites in the smears or thick drop preparations. The bilirubin content of the blood was 0.4 mg. per 100 ml. (icterus index 2). Blood urea was 53 mg. per 100 ml. Wassermann and Kahn reactions were negative. The patient weighed 130 lb. (58.97 kg.), having lost 28 lb. (12.7 kg.) in 26 days. Similar diet and multivitamin tablets were given as in Case 1.

*38th Day.*—The patient passed characteristic haemoglobinuric urine, sherry-red in colour, just after midnight. A second sample passed two hours later was lighter, and a third passed in the morning was almost normal. Subsequent samples were macroscopically normal, and before evening there was no spectroscopic evidence of oxyhaemoglobin in the urine. Constitutional symptoms and haemoglobinaemia in a sample of blood taken at 10 a.m. were conspicuous by their absence; the patient did not even have the little fever which occurred in Case 1. Spectroscopic examination of the blood showed only traces of oxyhaemoglobin, and there was no rise in the

icterus index. The blood count was not appreciably changed. The results of other tests as carried out in Case 1 were likewise all negative. Similar treatment was adopted.

*48th Day.*—The patient had an attack of severe abdominal pain below the umbilicus associated with tenderness in the right iliac fossa, vomiting, fever with rigor, and a leucocytosis of 13,200, with polymorphs 56%, lymphocytes 28%, monocytes 4%, and eosinophils 12%.

*60th Day.*—There were signs of improvement in the rigidity, tremor, and mental condition.

*66th Day.*—The patient complained of pain all over the body. He had haemoglobinuria again, and this time it was severer than that of Case 1. After midnight he passed three samples of very dark urine followed by urine of gradually diminishing colour. About twelve hours after the first sample was passed it had cleared considerably, but to the naked eye it was not completely clear until the evening. Once again there were no constitutional symptoms other than the preliminary aches and pains in the body, and no haemoglobinaemia about twelve hours after the first sample of haemoglobinuric urine, and the icterus index did not rise. The haemoglobin fell to 75%, and the red cells to 4,930,000 per c.mm. The white cells numbered 8,400 per c.mm., with polymorphs 68%, lymphocytes 23%, eosinophils 8%, and monocytes 1%. The results of blood smears and other tests carried out previously were all negative. Treatment similar to that in Case 1 was given; 10 ml. of concentrated antivenene was repeated next day also.

By the 80th day the patient had almost completely recovered, and on the 96th day he was discharged as fit.

A follow-up of both cases for twelve months showed that recovery was complete in all respects, and there had been no recurrence of haemoglobinuria.

## Discussion

In general petrol is a mixture of hydrocarbons of varying volatility and toxicity, the toxicity decreasing as the boiling-point increases. Octane, which is present in high proportion in some petrols, is very toxic—e.g., n-octane is about seven times as toxic as pentane (Lawrence, 1945). Some commercial petrols contain benzine and other aromatic hydrocarbons which are of still greater toxicity. The amount of lead tetra-ethyl is normally too small to be toxic, but, in circumstances to be discussed later, may give rise to lead-poisoning.

The toxic symptoms which arise after the inhalation of petrol vapour depend on the concentration of the vapour and the duration of exposure to it—e.g., Fieldner, Katz, and Kinney (1921) found that 1 part per 1,000 produced drowsiness in men after 15 minutes' exposure, and vertigo, ataxia, and nausea at the end of one hour, but 7 parts per 1,000 produced definite intoxication in five minutes. A very high concentration of the vapour causes almost immediate unconsciousness, and death from respiratory arrest (Rambousek, 1913).

Ordinarily, exposure to low concentration of vapour produces emotional changes simulating those of drunkenness. There may be excitement or euphoric exhilaration. Tolerance may be acquired by repeated exposure, and in such persons tremor of the hands without any emotional changes may alone occur on exposure to low concentrations of the vapour (Hamilton, 1925; Kulkow, 1926). Women may burst into fits of uncontrollable hysterical laughter or crying. Men may become irritable and quarrelsome.

Higher concentrations irritate the eyes, the skin, and the respiratory passages. A sense of constriction in the throat, burning pain in the chest and abdomen, a feeling of pressure over the heart, and irritation of the skin are followed by drowsiness, headache, vertigo, nausea, and muscular weakness. Tonic contractions of flexors of the hands and twitchings of the muscles of the trunk and limbs have been described at this stage by Rudd (1944).

With still higher concentrations the euphoric exhilarative period is very short. The patient becomes rapidly disorientated and abusive. Hallucinations may occur and he may defy rescue and become rapidly delirious and comatose. Convulsions may occur, but may be delayed till he is removed to fresh air for resuscitation (Machle, 1941).

From short exposures recovery is quick and is followed by deep slumber from which he can be roused. After prolonged exposure coma may last several days and end in death from respiratory failure. Recovery from coma may be heralded by muscular twitchings, and is usually associated with severe headache, vomiting, severe abdominal pain, pain in the extremities, extreme restlessness, and bursts of hysterical laughter. Headache, insomnia, loss of appetite, vomiting, pain in the extremities and abdomen, and muscular weakness are the usual immediate after-effects and may last several days. An early erysipelas-like eruption on the skin of the face and the mucous membrane of the mouth and throat followed by necrosis is an early and fatal complication that rarely occurs (Floret, 1927).

Sometimes damage inflicted on the nervous system gives rise after a variable period to symptoms simulating those of disseminated sclerosis or other organic nervous disease (Potts, 1915). The onset of epilepsy has been described by Floret (1927). Peripheral and cranial nerves may be involved, often singly, such as the sciatic (Jansen, 1937), hypoglossal, and optic. Recovery may take place or the nervous disability may be permanent. Lawrence (1945) recorded the occurrence of discomfort and tenderness in the right iliac fossa on the second day after exposure to petrol vapour, lasting till the twelfth day, without any abnormal amount of lead in the urine or faeces.

Lead tetra-ethyl is readily soluble in fats and oils, hence poisoning can occur by its absorption through the intact skin. The chief mode of absorption is, however, through the pulmonary epithelium from inhalation of its vaporized form, the amount absorbed being proportionate to the vapour pressure in the lung alveoli. As much as 5 mg. of lead per litre may be present in air saturated with its vapour, and the symptoms of poisoning are entirely due to this lead content. Owing to the solubility of lead tetra-ethyl in fats, however, the central nervous system is chiefly affected.

The concentration of lead tetra-ethyl in leaded petrol is usually not more than 1 in 3,000 by volume, and in this concentration the occurrence of lead-poisoning is unknown in workmen engaged in its distributive and allied trades, as well as among the general public (Kehoe, Thamann, and Cholak, 1934; Final Report of Departmental Committee, 1930; Lind, 1936). It is unlikely that lead tetra-ethyl plays any part in the symptomatology of acute petrol-vapour poisoning, except when the exposure is prolonged and the concentration of lead in the air is more than the safe limit of 1.5 mg. per 10 m.³ of air (American Public Health Association, 1943). Thus under controlled conditions, which keep the concentration below this limit, poisoning has hardly ever occurred in workmen engaged in the manufacture of the product and its blending with petrol (Kehoe, 1934; Kehoe and Machle, unpublished data, 1936).

No cases have been found in can-fillers and can-washers, although the urine has contained from 0.026 to 0.6 mg. of lead per litre (Cassells and Dodds, 1946).

These authors state that some of the men engaged in underground or semi-underground pump-houses, where the ventilation was poor and the concentration of the vapour naturally higher, however, showed mild symptoms of intoxication and a urinary lead concentration which was as high as 0.275 mg. per litre. Workers in depots built below the level of the surrounding countryside, and hence

with poor natural ventilation, showed a high urinary lead concentration but no symptoms of intoxication. However, 35 cases of poisoning are described in tank-cleaners who overlooked or disobeyed regulations governing the cleaning procedure. Machle (1935) had previously recorded 11 similar cases. In these the poisoning was due to inhalation of lead tetra-ethyl vapour in high concentrations rising out of the sludge or sediment deposited at the bottom of large tanks after storage for some time; these contained in analysed cases as much as 0.044 to 0.84% of organic lead compounds. Symptoms occurred after one to 17 days of exposure. "The classical signs and symptoms of lead-poisoning—namely, abdominal colic, tremors and fibrillary twitchings, myalgia, neuralgia, constipation, pallor, blue line on the gums, paralyses, stippling of the red blood cells, and punctate basophilia—either did not occur or were a very minor part indeed of the picture" (Cassells and Dodds, 1946), although in fatal cases the various organs showed a high concentration of lead—e.g., brain 0.6 to 0.74 mg., spleen 0.27 to 0.29 mg., liver 2.35 to 2.5 mg., kidneys 0.79 to 1.2 mg., against the normal maximum of brain 0.09 mg., spleen 0.07 mg., liver 0.28 mg., kidneys 0.16 mg. per 100 g. of wet tissue (American Public Health Association, 1943).

The earliest symptom was insomnia, with difficulty in falling asleep, broken sleep, and troubled dreams. Following this, and sometimes preceding it, came a nasty sweet taste in the mouth and halitosis, lack of appetite, nausea, vomiting, and diarrhoea with or without abdominal pain. Next in evidence were irritability, restlessness, nervousness, anxiety, difficulty in passing urine, and possibly tiredness. At this stage the pulse was slow, the temperature subnormal, the blood pressure diminished, and the reflexes increased, with the body weight showing slight loss. When exposure was longer and more severe "the signs and symptoms progressed to increasing tiredness and loss of body weight, tremor, muscular weakness and twitching, oddities of behaviour, and evidence of mental confusion, and then, quite abruptly, came the onset of acute maniacal symptoms with suicidal tendencies, or the occurrence of a convulsion" (Cassells and Dodds, 1946).

Although the classical signs and symptoms of lead-poisoning were absent urine examination showed a lead concentration which was usually above 0.15 mg. per litre. In fact, when the urinary lead concentration was less than 0.1 mg. per litre and symptoms of the above nature were displayed lead tetra-ethyl was considered unlikely to be the cause. The excretion of lead in the urine continued for a long time after exposure ceased, and sometimes the urinary concentration continued to rise in spite of cessation of exposure, to be followed by a progressive and gradual fall.

The clinical symptoms had apparently no relation to the urinary lead concentration—for in one of Cassells and Dodds's cases mental symptoms were present when the urinary lead concentration was 0.215 mg. per litre, but had disappeared later on when it had risen to 0.295 mg. Apparently loss of weight was sometimes very excessive, as shown in another of their cases by a gain in weight of 74 lb. (33.1 kg.) in about three months during the stage of recovery, and by a loss in a further case of between one and two stones (6-12 kg.) in about five weeks during the illness. Although the deep reflexes were usually exaggerated, at times they were diminished; in some cases they were exaggerated, while in others they were diminished—e.g., in one case "all reflexes were exaggerated except the biceps jerk, which was only just elicited." Cerebral symptoms in one case occurred suddenly in the midst of apparent recovery and ended fatally. There were no permanent sequelae: recollection of dreams was all that remained in one case.

Tropical conditions predispose to the occurrence of cases of lead tetra-ethyl poisoning. The two men whose cases are recorded in this paper were engaged, without any provision of airline masks or special clothing, in cleaning a tank which had not been rendered gas-free by ventilation after the petrol had been drained away. They thus faced a dual risk—one from the inhalation of petrol vapour, and the other from the absorption of lead tetra-ethyl by inhalation as well as by direct absorption through the intact skin.

The initial respiratory discomfort and irritation of the eyes were no doubt due to the effects of petrol vapour. It appears that sheer determination to work, associated with a fairly low concentration of the vapour, delayed the onset of giddiness, ataxia, and unconsciousness. To the effects of the same vapour may be ascribed the immediate symptoms, such as vertigo, headache, muscular weakness, anorexia, soreness of the eyes and throat, and pain in the lower limbs.

Symptoms of lead tetra-ethyl poisoning in a petrol-tank cleaner after exposure for a single working day have been described by Cassells and Dodds in one of the cases in their series, mentioned above. It will have to be conceded that these two workmen also absorbed enough lead during the day's exposure to give rise to such symptoms as marked loss of muscular power, muscular tenderness on pressure, and sluggish ankle- and knee-jerks due to its probable neuritic, muscular, spinal, or vasoconstrictor action. The numbness and the coldness of the lower limbs were perhaps due to vasoconstriction and the inability of the blood vessels to relax on account of the action of lead on them. Symptoms such as headache, anorexia, and body pains could be common to both effects.

Among the symptoms tremor, slow pulse, subnormal temperature, increased reflexes, loss of body weight, muscular weakness, and oddities of behaviour have all been described, as recorded above, in lead tetra-ethyl poisoning. It has been said that when symptoms of this nature are displayed lead tetra-ethyl is unlikely to be the cause if the urinary lead is less than 0.1 mg. per litre; yet on account of the similarity of symptoms it must be conceded that in my two cases these were due to lead tetra-ethyl in spite of failure to demonstrate pathological quantities of lead in the urine, and especially as in one of the cases there was no correlation between cerebral symptoms and the urinary lead concentration.

The unusual symptoms appearing in my two cases were:

1. *Acute Parkinsonism.*—As symptoms of organic nervous disorder are known to occur as sequelae of petrol-vapour poisoning it cannot altogether be ruled out that this was the case in these two patients. It is also known, however, that lead, through its vasoconstrictor action, can give rise to temporary blindness, angina pectoris, and gangrene of the extremities. Although localizing signs do not occur in lead encephalopathy, a similar selective action may play a part in the causation of acute Parkinsonism.

2. *Pain Simulating Acute Appendicitis.*—Discomfort and tenderness in the right iliac fossa, starting on the second day after exposure to petrol vapour and lasting until the twelfth day, recorded by Lawrence in one of his cases without any evidence of abnormal amounts of lead in the urine or faeces and apparently without any leucocytosis, bears a strong resemblance to an attack of similar pain in Case 2. However, in this instance it occurred 48 days after the exposure and was associated with a leucocytosis of 13,200 without a relative increase in the polymorphs. Such a leucocytosis is known to be associated with lead colic, and it is not impossible, therefore, that the appendicular reaction in this case was due to lead rather than to delayed effects of petrol vapour or to an incidental appendicitis.

3. *Haemoglobinuria.*—This apparently had all the clinical features of haemoglobinuria of exertion (Whitby and Britton, 1946). Its aetiology is obscure. Regarding the part played by exertion in these cases, all that can be said is that the patients were ambulant the previous day, but not to any great extent. Blood urea remained unraised and urine did not at any time before the onset of haemoglobinuria show evidence of nephritis or necrosing nephrosis due to toxic action of lead, or of haemoglobinuric nephrosis following haemoglobinuria. The possibility that it was caused by an acute haemolytic crisis due to lead cannot be ruled out. It appears that the blood was almost completely cleared of its oxyhaemoglobin content when a sample was taken for examination, whereas the urine collected at the same time was that which had accumulated in the bladder for at least four hours. Subsequent samples of urine had been markedly and progressively clear. The amount of blood destroyed by haemolysis seems to have been small, as shown by the red-cell counts before and after the haemolysis. The first sample of haemoglobinuric urine had been passed from seven to nine hours before the collection of venous blood. Haemolysis had no doubt taken place earlier than this. During this period the haemoglobin in the blood could have been easily cleared by the kidneys. Hence the apparent similarity to haemoglobinuria of exertion.

4. *Erythrocytosis.*—This accompanied the symptoms of acute Parkinsonism very closely. In all probability it was of the same nature as polycythaemia described in encephalitis lethargica and Huntington's chorea by Moehlig and Bates (1933).

5. *Pallor.*—This was not a feature of any of the cases recorded by Cassells and Dodds. Its presence in my two cases was a pointer to its causation by lead.


## Summary

Acute Parkinsonism, haemoglobinuria, abdominal pain simulating appendicitis, erythrocytosis, and pallor are recorded in two petrol-tank cleaners. These symptoms were in addition to the usual effects of exposure to petrol vapour and lead tetraethyl.


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Mr. Lawrence B. Hall, sanitary engineer of the U.S. Public Health Service, has gone to Iran to help in that country's fight against malaria. He will continue work in malaria control initiated by another Public Health Service officer, Dr. Justin M. Andrews, and will supervise training of Iranian personnel in carrying out a D.D.T. spraying scheme recommended by Dr. Andrews after a survey a few months ago. Mr. Hall's headquarters will be in Tehran. The Iranian Embassy in Washington requested the services of Mr. Hall under terms of the Smith-Mundt Act, an educational exchange programme through which the U.S.A. gives technical and other services on a reciprocal basis with other nations. Mr. Hall did malaria-control work along the Burma Road in 1941, and also later when he was attached to the China-Burma-India Command of the U.S. Army.

# STAPHYLOCOCCI IN THE NEWBORN

## THEIR COAGULASE PRODUCTION AND RESISTANCE TO PENICILLIN AND STREPTOMYCIN


BY

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This investigation was undertaken to determine the incidence of staphylococci in the nasopharynx and the faeces of normal infants during the first seven days of life. Potentially pathogenic strains were differentiated by the coagulase method and their sensitivity to penicillin and streptomycin was tested. The results refer to infants born in hospital and may not perhaps be applicable to newborn infants generally. They are, however, a contribution to the study of the oecology of the staphylococcus both with regard to the newborn and in relation to possible effects of antibiotics on staphylococci in the whole community.

Although numerous studies and reviews of the respiratory and faecal flora of normal infants are available there is little information about the incidence of staphylococci during the first week of life.

Torrey and Reese (1945) found carrier rates of haemolytic *Staph. aureus* of 6.6% during the first day, 50% for the second day, 62% for the third day, and 88.8% during the fourth to eighth days. Kneeland (1930) found in 30 normal infants during the first two weeks of life an incidence of 93% of *Staph. albus* and 32% *Staph. aureus*. Todd (1922) cultured dried powdered stools on human blood agar from infants and obtained *Staph. albus* in 53% ; *Staph. aureus* was not found. Crowley, Downie, Fulton, and Wilson (1941) found in 57 normal breast-fed infants, 3–23 days of age, that about 50% had *Staph. albus* in the stools ; *Staph. aureus* was present only once.

### Technique

The infants studied were born in the obstetrical department of St. Mary's Hospital, Manchester, and were in five nurseries each containing a maximum of 12 cots. They were all healthy, full-term, breast-fed, and in contact with their mothers only at feeding-times. None had been treated with penicillin, and so far as could be ascertained none of the mothers had received any. No persons in contact with the children wore masks. Visitors were not allowed in the nurseries. There was no special air-conditioning in the nurseries. The survey was made from August to November, 1948.

Specimens were taken from the nasopharynx by means of per-nasal swabs—i.e., fine cotton-wool swabs on thin flexible iron wire passed via the external nares to the back of the nose. Rectal swabs were taken, using adult-type throat swabs, with special precautions against contamination from the skin surrounding the anus.

The nasal swabs were plated on horse-blood agar within one to two hours of collection and incubated aerobically at 37° C. The rectal swabs were plated on horse-blood agar and MacConkey's bile-salt medium and inoculated into 10% NaCl in Robertson's meat medium as recommended by Maitland and Martyn (1949) for the selective isolation of staphylococci. The culture from the salt-meat medium after incubation aerobically for twenty-four hours at 37° C. was subcultured to horse-blood-agar plates, also incubated for twenty-four hours. It was not necessary to use the selective medium for nasal swabs, as the staphylococci were not mixed with many other bacteria.

When the colonies were uniform in colour on one plate one colony only was subcultured. If there was more than

one variety a colony of each was picked. As the main object was to determine the incidence of coagulase-positive strains, if an aureus colony turned out to be coagulase-negative the plate, which had been kept, was re-examined and other colonies picked—a procedure which sometimes led to the isolation of a coagulase-positive strain. Such a plate was then recorded as having two varieties of staphylococci. All strains isolated were tested for the production of coagulase, 0.5 ml. of a 1 in 10 dilution of citrated human plasma being used and 5 drops (approximately 0.125 ml.) of an overnight broth culture being added. The culture was incubated at 37° C., and examined after two hours and after standing at room temperature overnight. All coagulase-positive strains are referred to as *Staph. pyogenes*, and the great majority of them had aureus colonies. The coagulase-negative strains are designated *Staph. saprophyticus*; they usually had white or nearly white colonies, and no attempt was made to differentiate strains which morphologically might have been classed as micrococci.

### Results of Culture

Cultures were made from 130 infants, and the results are summarized in Table I. From the nasopharynx, apart

TABLE I.—*Incidence of Staphylococci Isolated from Nasopharynx and Faeces of 130 Healthy Infants Aged 0–7 Days*

| | All Sources | Naso-pharynx (total) | Faeces (total) | Naso-pharynx and Faeces | Naso-pharynx Only | Faeces Only |
|---|---|---|---|---|---|---|
| *Staphylococcus* .. | 130 (100%) | 127 | 130 | 127 | 0 | 3 |
| *Staph. pyogenes* .. | 99 (76%) | 81 (62%) | 65 (50%) | 47 (36%) | 34 (26%) | 18 (14%) |
| *Staph. saprophyticus** | 112 (86%) | 70 (54%) | 102 (78%) | 60 (46%) | 10 (8%) | 42 (32%) |

* Micrococci were not differentiated (see text).

from three infants a few hours old whose swabs yielded no growth, staphylococcus was always present, and usually it was the only organism. As a rule it appeared as a pure aureus or albus strain, but sometimes there was more than one variety. *Streptococcus viridans* was noted in a few cases. Other bacteria were few, and were not identified.

The isolation of staphylococci from the faeces of all infants was the result of using a selective medium which has been shown by Maitland and Martyn to detect small numbers. Direct plating of the same rectal swabs on blood agar seldom revealed staphylococci. The high incidence of 50% for *Staph. pyogenes* in the faeces of normal infants is noteworthy.

### Penicillin and Streptomycin Sensitivity of Coagulase-positive Strains Isolated

Barber and Rozwadowska-Dowzenko (1948) have stated that the incidence of penicillin-resistant staphylococci cultured from infections has been increasing during the past few years. The coagulase-positive staphylococci isolated from normal healthy infants were therefore tested for sensitivity to penicillin to see if the relatively high incidence of penicillin-resistant strains was peculiar to infections. The opportunity was taken to test the strains as well for sensitivity to streptomycin.

*Methods.*—Penicillin sensitivity was tested by soaking strips of sterile filter-paper (about 7 by 1 cm.) in normal saline containing 40 units of crystalline penicillin per ml. A strip was then laid on a nutrient-agar plate after it had been inoculated in streaks with eighteen-hour broth cultures of the staphylococci to be tested. The Oxford staphylococcus was inoculated on every plate as a control. Resistant strains detected by this method were tested for the production of penicillinase by mixing equal volumes of an overnight broth culture and normal saline containing 5 units of penicillin per ml. Each mixture was then tested by the cylinder-plate method for the presence of penicillin by the technique described by Hayes (1945). Streptomycin sensitivity was similarly tested with strips soaked in a concentration of 1,000 units per ml. of streptomycin.

TABLE II.—*Penicillin and Streptomycin Sensitivity of Strains of Staph. Pyogenes Isolated from Nasopharynx and Faeces of Healthy Infants Aged 0–7 Days*

| Source: | Nasopharynx | Faeces |
|---|---|---|
| Total No. of *Staph. pyogenes* isolated .. | 81 | 65 |
| No. of penicillin-resistant strains .. .. | 45 (55·5%) | 38 (58·5%) |
| No. of streptomycin-resistant strains .. .. | 3 (3·7%) | 1 (1·5%) |

*Results.*—In Table II are shown the numbers of strains isolated from the nasopharynx and faeces which were resistant to penicillin and streptomycin. The incidence of 55.5% of strains resistant to penicillin in the nasopharynx and of 58.5% in the faeces approximated very closely to the incidence recorded by Barber and Rozwadowska-Dowzenko of 59% in infections. All the 83 penicillin-resistant strains produced penicillinase, but three strains failed to show it by the standard test against 5 units of penicillin per ml. It was shown for these three strains, however, by using 1 unit of penicillin per ml. The incidence of streptomycin-resistant strains was low. Only four such strains were encountered, and they were all sensitive to penicillin.

### Uniformity of Strains from Individual Cases

To test the possibility that what appeared to be a pure culture of *Staph. pyogenes* might be a mixture of penicillin-sensitive and penicillin-resistant strains 20 colonies were picked from each of five plates and tested separately. Three plates were from faeces and two from the nasopharynx. All the colonies from each plate were similar: the strains were penicillin-resistant.

Further evidence regarding uniformity of strains was obtained by testing for sensitivity to penicillin and streptomycin pairs of strains, one from the nasopharynx and one from the faeces of individual infants. There were 47 such pairs—37 were similar, 8 were different in their sensitivity to penicillin, and 2 others differed in sensitivity to streptomycin, in each instance one strain being sensitive and the other resistant according to the method of testing.

The fact that in about three-quarters of the infants harbouring *Staph. pyogenes* in both nasopharynx and bowel the strains were similar in their behaviour to antibiotics may be regarded as suggestive evidence of their common origin and in favour of their uniformity. Against this should be put the observation that in about one-quarter of the infants the strains from bowel and nasopharynx were different in sensitivity to antibiotics. To obtain complete evidence regarding the degree of uniformity in the staphylococcal flora of very young infants bacteriophage typing of a number of strains from each source should be undertaken. So far as penicillin resistance is concerned the evidence obtained in this investigation suggests that examination of one colony from each source did not introduce a large error owing to lack of uniformity in the flora.

### Comment

The staphylococci found in young infants are derived from the environment, and the incidence and variety of staphylococci found may therefore be expected to vary somewhat in different groups.

In the present investigation in a maternity hospital the relative importance of the mothers, of attendants, and of the air of the wards as a source of staphylococci is

not known. The incidence of 62% of *Staph. pyogenes* in the nasopharynx and its relative predominance is not unexpected in view of the findings of others (Kneeland, 1930; Torrey and Reese, 1945). The high incidence of 50% in the faeces is much greater than has been recorded heretofore (Todd, 1922; Crowley, Downie, Fulton, and Wilson, 1941), owing largely, it is believed, to the selective medium employed. It is a relevant point in considering the staphylococcus as a possible aetiological agent in enteritis.

The high incidence of penicillin-resistant strains in both nasopharynx and bowel probably reflects the strains circulating in a hospital environment. It is of interest that a similar incidence was found by Barber and Rozwadowska-Dowzenko (1948) from strains from infections, also in hospital. The figures obtained from this series of infants, taken in conjunction with time and place, may be regarded as a contribution to the further study of penicillin resistance of staphylococci in the community.


### Summary

An investigation into the incidence of staphylococci in the nasopharynx and faeces of 130 normal healthy breast-fed infants aged 0–7 days born in the Maternity Department of St. Mary's Hospital, Manchester, is recorded.

From the nasopharynx *Staph. pyogenes* was isolated in 62% of the infants and from the faeces in 50%.

Of the *Staph. pyogenes* strains isolated from the nasopharynx 55.5%, and from the faeces 58.5%, were penicillin-resistant. All the resistant strains produced penicillinase.

Only four strains of *Staph. pyogenes* isolated were resistant to streptomycin.

In the cases that were specially tested there was homogeneity in the staphylococcal flora of the nasopharynx and bowel in individual infants so far as sensitivity to penicillin was concerned. In three-quarters of the infants who harboured *Staph. pyogenes* in both nasopharynx and bowel the strains from the two sources corresponded in their susceptibility to both penicillin and streptomycin.

The high incidence of *Staph. pyogenes* in the faeces was due largely to the use of a selective medium, and the high incidence of penicillin-resistant strains probably reflects the strain circulating in the hospital.


I wish to thank Professor W. F. Gaisford for his interest and advice and Professor H. B. Maitland for helpful criticism.

This work was undertaken whilst holding the Cow and Gate Research Fellowship in Child Health tenable in the Department of Child Health, University of Manchester.

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The Ministry of Health has issued a circular describing the procedure to be followed in caring for persons of unsound mind arriving at seaports and airports. If a British subject of unsound mind is not met by a relative or friend who will take charge of him, the medical officer there should call in the appropriate duly authorized officer of the local health authority, who is responsible for removing a person of unsound mind. An alien of unsound mind is prohibited by the Aliens Order, 1920, from being given leave to land, but Article 14 of the Order enables the Secretary of State to exempt any person from that prohibition. An immigration officer who considers that an alien is of unsound mind should seek the advice of the Medical Inspector of Aliens. If the latter is satisfied that the alien is of unsound mind, he gives the appropriate certificate on Form Port 12 to the immigration officer. If, nevertheless, the alien is allowed to land, the immigration officer is responsible for his disposal, and he may then deal with him in the same way as for a British subject.

# Medical Memorandum

## Unusual Physical Signs in Strangulated Inguinal Hernia

The following case of strangulated inguinal hernia is recorded because it illustrates three physical signs which should receive wider recognition.

### Case Report

A normal healthy man aged 33 was admitted to hospital complaining of a swelling in the right groin and vague abdominal pain. The swelling in the groin had been present for about six weeks and had not given rise to any symptoms until three days before admission, when it became painful and enlarged rapidly, extending into the scrotum. He complained of some generalized abdominal pain of colicky nature, a little nausea, and constipation for two days. It was also reported that blood-stained fluid had been aspirated from a hydrocele on the right side some hours previous to admission.

On examination a large fusiform swelling was seen in the right groin, extending downwards and continuous with a very large swelling in the right half of the scrotum. It was impossible to get above the swelling in the groin, yet the swelling of the scrotum was clearly cystic and translucent, although not brightly so. There was a good cough impulse over the swelling in the groin. Auscultation of the abdomen revealed some increase of peristaltic sounds, and the heart sounds could be clearly heard throughout the whole abdomen.

At operation a loop of ileum was found to be strangulated at a constriction about half-way down an hourglass-shaped hernial sac. About 6 in. (15 cm.) of bowel was involved, and the distal sac, which was very large, was filled with dark blood-stained fluid. Considerable ascites was present in the abdominal cavity, with moderate intestinal distension.

The strangulated bowel was thickened, waterlogged, and dark purple in colour, and the mesentery was thrombotic and oedematous. After the usual measures to restore the circulation it was decided to resect the bowel, and a piece about 2 ft. 6 in. (76 cm.) was removed and an end-to-end anastomosis performed. The large congenital sac was removed and the hernia repaired. The patient made an uninterrupted recovery and at a follow-up three months later had no complaints.

### Commentary

*The Cough Impulse.*—In a case of suspected strangulated hernia the presence of a cough impulse should not necessarily rule out the diagnosis. As in this case, the site of strangulation may be some way distal to the external abdominal ring, leaving the proximal part of the contents unstrangulated.

*Blood-stained Hydrocele.*—The collection of blood-stained fluid from a hydrocele is usually considered to be associated with some disease or trauma of the testis. The above case demonstrated that it may be associated with intestinal obstruction. Such a finding was of even greater interest in another case I had some years ago. A man presented with a recently developed hydrocele of a hernial sac with blood-stained fluid. On lying the patient down it was found that the sac could be slowly emptied into the peritoneal cavity—i.e., the processus vaginalis was patent. At operation an internal strangulation due to a fibrous band was found. At no time had he ever noticed any descent into the hernia—the congenital sac being always there, but making itself manifest only when blood-stained fluid formed within the abdomen.

*Heart Sounds Heard Clearly in the Abdomen.*—This fact, I believe, signifies a combination of intestinal distension and fluid. I have heard the sounds on other occasions, and these findings have always been confirmed at operation or strongly supported by other signs.

In the case recorded the fluid in the abdomen was no doubt present because the strangulation was of that type which starts with slow venous occlusion, as shown by the thickened waterlogged loop of strangulated bowel in contrast to the thin friable type of wall found in more rapid strangulation in which the arteries are quickly occluded. Although in the former type of obstruction I believe the bowel is often more viable than its appearance would suggest, it is this type of strangulation which leads to late obstruction from interstitial fibrosis and constriction if the bowel is dropped back.

If the patient's condition warrants it, an immediate resection would always seem justified.

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# Reviews

## CARE OF CHILDREN

*Advances in Pediatrics.* Volume 3. Edited by S. Z. Levine, A. M. Butler, L. E. Holt, jun., and A. A. Weech. (Pp. 363; illustrated. £2 5s.) New York and London: Interscience Publishers. 1948.

*Handbook of Parentcraft.* By Leslie George Housden, O.B.E., M.D. With an Introduction by Sir Wilson Jameson, K.C.B., F.R.C.P., D.P.H. (Pp. 152. 5s.) London: Eyre and Spottiswoode, 1948.

The third volume of *Advances in Pediatrics* is up to the high standard set by its predecessors. Eight monographs, each with useful bibliographies, cover a wide range of interests. It is significant of the present-day trend that two of the eight are on psychological matters. The account of the treatment of epilepsy and the social management of children with this complaint is a practical contribution of great importance. A thoughtful essay on the effects of birth processes and obstetric procedures on the newborn infant is a worthy product of the Boston School, from which comes also an account of retrolental fibroplasia, posthumously contributed. From Philadelphia the pen of an expert deals with viral hepatitis, and the contribution from Johns Hopkins is on abnormalities of sexual development, a study which was presented in graphic form at the International Congress on Pediatrics in 1947 in New York. A concluding essay on the osteochondroses is a comprehensive account of this curious group of bony abnormalities. The reviewer's only regret is that a year must elapse before more surveys of this type are available.

Dr. L. G. Housden's little volume on parentcraft makes available in permanent form the teachings of this keen enthusiast. His general thesis is perhaps sounder than some of his details. Pasteurized milk is not generally regarded as safe for babies without boiling, and the milk dilutions advocated (with the briefest mention of dried milk) are not those generally accepted. However, Dr. Housden's object is to educate young parents in their job, which is a larger and more important theme than bottle feeding, and he has certainly succeeded in writing an interesting book.

ALAN MONCRIEFF.

## PSYCHOLOGY OF CHILDREN

*Childhood and After. Some Essays and Clinical Studies.* By Susan Isaacs, C.B.E., M.A., D.Sc.(Vict.), Hon.D.Sc. (Adelaide). (Pp. 245. 15s.) London: Routledge and Kegan Paul. 1948.

With the death of Susan Isaacs we have lost one of the foremost pioneers of child psychology and one whose originality of thought and powers of observation are all too uncommon in this or any other field of mental science. An early adherent of the psycho-analytic school, she may have been regarded by some as too extreme in her early days, but later she became a wise counsellor whose knowledge and understanding of the inner workings of the human mind made her a real help to the community.

This development is reflected in this book, which is a collection of lectures and addresses some of which have not previously been published. One of the early essays—that on privation and guilt (1929)—is full of the extreme Freudian ideas —the Oedipus complex, the castration complex, infantile sadism, and so on. That there are at times waves of hostility to the mother and still more to the father in the mind of the young child, and that these moods may influence subsequent behaviour, may readily be accepted, but that specific desires to tear the mother to pieces, to destroy her and eat her, are ever formulated even in the deepest layer of the unconscious is less credible, though the hostility may later be expressed in some such way during psychotic fantasies. In a later essay (1940) on temper tantrums we find a less extreme attitude when the author is discussing tantrums in young children, but she returns to somewhat extravagant Freudian explanations in respect of the emotional outbursts of a young schizoid adult.

The last two essays—on fatherless children and children in institutions—are wholly admirable—sensible, instructive, and constructive. The last is the full text of a memorandum to the Curtis Committee and must have influenced and impressed that body considerably. This volume is of great interest in showing the development not only of the author's mind but also of the whole modern attitude to abnormal psychology.

R. G. GORDON.

## HODGKIN'S DISEASE

*Hodgkin's Disease and Allied Disorders.* By Henry Jackson, jun., A.B., M.D., and Frederic Parker, jun., A.B., M.D., Oxford Medical Publications. (Pp. 177; 14 plates. £2 5s.) New York: Oxford University Press (Geoffrey Cumberlege). 1947.

This attractively produced monograph embodies the authors' observations on a series of 259 cases of Hodgkin's disease. The "allied disorders" discussed successively in shorter sections are reticulum-cell sarcoma, giant-follicle lymphoma, lymphocytoma, lymphosarcoma, plasmocytoma, and endothelioma. The authors describe all these conditions from their combined clinical and pathological aspects and illustrate them by radiographs and photomicrographs.

While the text is full of interesting and authoritative observations which will be of value to the practising specialist and pathologist, there is nothing revolutionary in these pages. The most controversial aspect of the account of Hodgkin's disease perhaps lies in their distinguishing three forms of the condition —paragranuloma, granuloma, and sarcoma. The authors consider that each of these displays a distinctive pathological and clinical picture. While "paragranuloma" has been regarded by others as "early Hodgkin's disease," the authors claim that, although it may pass on to the granuloma phase, it may persist unchanged for many years, and they quote an instance where the patient is alive and active 39 years after the diagnosis was established by biopsy. The paragranuloma and granuloma together conform to the prevailing conception of Hodgkin's disease. It may be, however, that some examples at least of the paragranuloma are rather to be regarded as the equivalent of Robb-Smith's lympho-reticular medullary reticulosis.

The interpretation of what is called Hodgkin's sarcoma is a difficulty that confronts all pathologists; we read (p. 32) that the spleen was involved in only 9 of 32 cases, but it seems likely that this group would be broken down by other authorities into different categories. Doubtless this and other controversial points will be resolved only when the aetiology of the disease is known.

DOROTHY S. RUSSELL.

## ANALYTICAL PSYCHOLOGY

*Studies in Analytical Psychology.* By Gerhard Adler, Ph.D. (Pp. 209; illustrated. 21s.) London: Routledge and Kegan Paul. 1948.

The contributions of C. G. Jung to psychiatry and psychopathology are so extensive that a summary of some main concepts is welcome. The summary presented in this volume is given in the setting of clinical experience, and in consequence the account is vivid and avoids the dullness of an epitome. It is not a book for the beginner. Throughout the author assumes that the reader is familiar with the terminology of analytical psychology and psycho-analysis.

In the opening chapter, "A Comparative Study of Analytical Psychology," the author criticizes chiefly the Freudian point of view, and he competently discusses the differences between the teaching of Jung and of Freud. The exposition of Jungian theory and clinical procedure in the later chapters is more useful and gives the book its practical value. Psychiatrists have the unusual opportunity of observing a colleague at work and noting just how he tackles the well-known problems. Now and then, however, the author's enthusiasm outruns his critical faculty and we find a tendency to generalize from particular instances. It is probably true, for example, that some—perhaps many—children go through ceremonies with their dolls and animal toys before going to sleep in order to allay dimly felt anxiety of the powers of darkness. But not every child is afraid of the dark, and not every child who says good night to its doll is carrying out a protective ceremony customary in primitive races (p. 101).

Drawing and painting have been used for years in psychiatry as a form of diversional therapy, but their use in expressing

hitherto unrecognized thought and feeling, for which no other vehicle will serve, is more recent. The illustrations in this volume, drawn by the author's patients in an attempt to understand their dreams, are of this type, and the commentary upon them is clear and informative. The final chapter, on "Jung's Contribution to Modern Consciousness," takes us beyond the limitations of psychiatry and describes how much psychology as a whole has gained by Jung's teaching. The book is worthy of serious attention and will be of special interest to post-graduate students who require a lucid statement on such subjects as symbolism, the collective unconscious, archetypes, amplification, the opposites, and dream analysis.

E. A. BENNET.

## TELEKINESIS

*The Reach of the Mind.* By J. B. Rhine. (Pp. 188. 10s. 6d.) London: Faber and Faber. 1948.

Psychology is indebted to Professor Rhine for his pioneer scientific work on telepathy, clairvoyance, and, most recently, telekinesis. This work, extensively confirmed elsewhere, could not be seriously discussed until the combination of controlled experiment and statistical analysis showed, as it now has done, that effects are being obtained which cannot be accounted for by any present theory of mental and physical interaction. They demand further inquiry. The late Sir James Jeans once remarked that any experiment should be regarded with the greatest caution until it was confirmed by theory. This is the present standing of these studies of "psi" phenomena. The reader receives the impression that Professor Rhine is studiously avoiding the statement of any working hypothesis and that he is best pleased when the results of experiment are apparently senseless.

He has, for instance, performed a great number of experiments on the power of his subjects to influence the fall of rolling dice, and he shows that they can at will secure an excessive proportion of high or of low numbers on the top faces of the dice when they have come to rest. He has experimented with dice of various shapes—e.g., with sharp or rounded edges—and found no difference between them. Telekinesis is unaffected by such mechanical factors. He also says, however, that he gave up experimenting with disks because he got no statistically significant results; so it seems that the shape of these experimental objects does have some effect after all. If mental operations have some direct effect on isolated physical systems, then they must be to some extent subject to the laws of physics; if Professor Rhine has not found this, it may be because he has not looked in the right direction. If his views are correct, there is no reason why the pure willing of one of his subjects should not be able to roll over a single dice after it has come to rest and turn it so as to show another face. A single successful experiment of this kind would be a clearer demonstration to the vulgar than a thousand experiments whose validity depends on statistical analysis.

Professor Rhine is enthusiastically concerned to demonstrate the paramountcy of mind and the "psychocentric" nature of man, as well as to dethrone materialist systems of philosophy. Although the phenomena he reports are extremely interesting, their theoretical interpretation is still so doubtful that no radical change in the basic philosophy of science seems yet to be called for.

ELIOT SLATER.

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Dr. Frederick Christopher's *Minor Surgery* (sixth edition, pp. 1,058; 937 illustrations on 595 figures; £3. Philadelphia and London: W. B. Saunders) includes much more than is usually found in the house-surgeon's manual. As the author points out, the distinction between minor and major surgery is at times almost impossible to make. He has overcome this difficulty by giving the term a comprehensive meaning. As a result the book will be useful not only to the newly elected house-officer but to the majority of practitioners and assistant surgeons. This edition has been brought thoroughly up to date. Indeed, the author considers such procedures as the use of oxidized cellulose for the control of haemorrhage and others which have not yet established themselves, but he always gives references to recent work. The chapters on the surgery of the extremities make the book a useful treatise on minor orthopaedic work—perhaps as good as is to be found anywhere. This book has always been popular; in its new revised form it is likely to be more so.

## BOOKS RECEIVED

*[Review is not precluded by notice here of books recently received]*

***A Course in Practical Therapeutics.*** By M. E. Rehfuss, M.D., F.A.C.P., and others. (Pp. 824 82s 6d.) London: Bailliere, Tindall and Cox. 1948.

Systematically arranged and fully illustrated.

***The Diagnosis of the Acute Abdomen in Rhyme.*** By Zeta. 2nd ed. (Pp. 93. 6s.) London: H. K. Lewis 1949.

A second edition of the well-known epic.

***An Introduction to Public Health.*** By E. W. Caryl Thomas, M.D., B.Sc., D.P.H. (Pp. 263. 15s.) London: Simpkin Marshall. 1949.

A short book for students.

***Cunningham's Manual of Practical Anatomy.*** By J. C. Brash, *M.C.*, M.A., M.D., F.R.C.S.Ed., F.R.S.Ed. Vol. 1. 11th ed. (Pp. 387. 21s.) London: Geoffrey Cumberlege. 1948.

General introduction, and the upper and lower limbs

***Pediatric Anesthesia.*** By M. D. Leigh, M.D., and M. K. Belton, M.D. (Pp. 240. 27s. 6d.) London: Macmillan. 1948.

Theory and practice of anaesthesia for children

***Eat and Grow Beautiful.*** By G. Hauser. (Pp 233. 9s. 6d.) London: Faber and Faber. 1949

A book for the non-scientific reader.

***Practical Orthoptics in the Treatment of Squint.*** By T. K. Lyle, M.A., M.D., M.Chir., M.R.C.P., F.R.C.S., and S. Jackson, S.R.N., D.B.O. 3rd ed. (Pp. 271. 35s.) London: H. K. Lewis 1949.

An extensively revised edition.

***Common Sense About Hair.*** By G. Reeson, M.I.T., and C. Bedeman, M.I.T. (Pp. 78. 3s. 6d.) London: Walding Press. 1949.

For the layman.

***Psycho-Analysis Today.*** Edited by S. Lorand, M.D. (Pp. 404. 25s.) London: George Allen and Unwin. 1948.

A survey of the development of psycho-analysis.

***La Marihuana en la America Latina.*** By P. O Wolff (Pp. 55. No price.) Buenos Aires: El Ateneo. 1948.

Extended version of a lecture given to the Medico-Legal Society of Buenos Aires.

***The Neurosis of Man.*** By T. Burrow, M.D., Ph.D. (Pp. 428. 28s.) London: Routledge and Kegan Paul. 1949.

An analysis of the causes of neurosis.

***Klinische Infektionslehre.*** By F. O. Höring. 2nd ed. (Pp. 245. M. 18.) Berlin: Springer. 1948.

A study of the pathogenesis of infection.

***Index-Catalogue of the Library of the Surgeon-General's Office United States Army.*** Edited by C. F. Mayer, M.D. (Pp. 994. $4.25.) Washington: U.S. Government Printing Office. 1948.

The tenth volume of the fourth series, which is also the fifty-seventh volume of the entire publication since its inception in 1880.

***Anaesthetics and the Patient.*** By G. Ostlere, D.A. (Pp. 166. 7s. 6d.) London: Sigma Books. 1949.

A monograph for nurses, junior medical students, and the layman.

***Yearbook of General Surgery, 1948.*** Edited by E. A. Graham, M.D. (Pp. 717. 25s.) London: H. K. Lewis. 1949.

A review of the year's literature.

***First Steps in Childhood.*** By G. M. Kerr, M.B., B.S., D.A. (Pp. 120. 3s. 6d.) London: Clerke and Cockeran. 1949.

For mothers.

***Tuberculosis of the Knee-Joint.*** By J. Mortens. (Pp. 550. Kr. 30.) London: H. K. Lewis. 1948.

English translation of a recent Danish monograph.

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## THE SYMPATHETIC TRANSMITTER

Adrenaline is an amine in which one hydrogen atom is replaced by a methyl group; the same amine in which this hydrogen atom is not replaced is known as nor-adrenaline or arterenol. Evidence is accumulating to show that the substance which transmits sympathetic impulses to the end organ is nor-adrenaline, and not adrenaline as many have thought: several workers[1-4] have obtained results indicating that nor-adrenaline is the transmitter at sympathetic nerve endings in the liver. Recently von Euler[5] has demonstrated by colorimetric and biological tests that extracts of sympathetic splenic nerve fibres of cattle contain l-nor-adrenaline—a finding which again emphasizes the importance of this substance. To be set in the balance against this evidence is that of Gaddum and his colleagues,[6 7] who found the substance liberated by the stimulation of sympathetic nerves to the vessels of the rabbit's ear to be adrenaline.

All this work might seem at first sight to be of academic importance only, but Goldenberg and his colleagues[8] in the U.S.A. have been quick to see its possible clinical significance. They have made a clinical study of the effects of intravenous infusion of nor-adrenaline, comparing them with those of adrenaline. The vasodilator effect of adrenaline has been demonstrated in man by Allen, Barcroft, and Edholm[9] and by other workers.[10-12] The action of nor-adrenaline is different: intravenous infusion causes vasoconstriction and a rise in pressure. For example, in one patient Goldenberg and his colleagues found that infusion of adrenaline caused a fall in the total peripheral resistance (expressed in dynes cm.$^{-5}$ sec.) from 1,000 to 500; the infusion of nor-adrenaline on the other hand caused a rise from 1,250 to 1,750. When both adrenaline and nor-adrenaline were infused there was a fall; the presence of adrenaline appeared to block the constrictor action of nor-adrenaline. From these and similar observations in other patients they put forward the highly speculative theory that essential hypertension may be considered to be a disease of deficient transmethylation, though they admit that their study provides no "definitive evidence" for this view. They suggest, that is, that nor-adrenaline is a precursor of adrenaline, and that essential hypertension results from a failure to effect the conversion. Recently Holtz and Kroneberg[13] put forward the view that epinine rather than nor-adrenaline is the precursor of adrenaline. Obviously, until there is evidence that nor-adrenaline can become adrenaline by methylation, the theory, however interesting, must remain insecure. The difference between nor-adrenaline and adrenaline is not confined to the action on the vessels, for Barcroft and Konzett[14] have shown that intravenous infusion in man of nor-adrenaline causes a slowing of the heart rate, while that of adrenaline causes a quickening.

If nor-adrenaline is the sympathetic transmitter and is a purely constrictor substance, how then is sympathetic vasodilatation to be explained? It has been known since the time of Dastre and Morat[15] that the stimulation of certain sympathetic fibres produces vasodilatation. The experiments of Bülbring and Burn[16] threw light on sympathetic vasodilatation in the dog. They found that the vasodilatation was due to the liberation of acetylcholine. Folkow and Uvnäs[17] in Sweden have now studied sympathetic vasodilatation in the cat and have come to the conclusion that in this animal as well as in the dog the transmitter is acetylcholine. They and their colleagues[18] have also shown that the sympathetic vasodilator fibres in the coronary vessels liberate acetylcholine. They regard nor-adrenaline as the transmitter of all constrictor impulses in the cat and acetylcholine as the transmitter of all sympathetic dilator impulses.

The most recent observations on nor-adrenaline concern the medulla of the suprarenal gland. Holton[19] has shown that medullary tumours contain much more nor-adrenaline than adrenaline. Meier and Bein[20] have found that the dilator action of adrenaline on the limb vessels disappears if the suprarenal glands are removed, but it reappears if nor-adrenaline is infused intravenously; thus they suppose that the suprarenal medulla must liberate not only adrenaline but also nor-adrenaline. Schümann[21] has reported the presence of nor-adrenaline in the suprarenal of the pig. Bülbring and Burn[22] have shown that stimulation of the splanchnic nerve in the cat liberates from the suprarenal medulla a mixture of nor-adrenaline and adrenaline—on an average about 50% of each. Thus nor-adrenaline is rapidly becoming a substance of unexpected importance, and the rate at which new discoveries in this field are appearing is so great that conclusions of clinical interest seem bound to emerge very soon.

## DIPHTHERIA PROPHYLACTICS

From 1911 to 1940 the number of cases of diphtheria notified in England and Wales was consistently round about 50,000 a year. In 1940 the Ministry of Health introduced its immunization scheme—the prophylactic most commonly used being alum-precipitated toxoid (A.P.T.)—and in 1942 the number of notified cases was 41,404; after that it fell steadily—34,662 in 1943, 29,949 in 1944, 18,596 in 1945, 11,986 in 1946, and 3,941 in 1947, the last year

1 Stehle, R. L., and Ellsworth, H. C., *J. Pharmacol.*, 1937, **59**, 114.
2 Greer, C. M., *et al.*, ibid., 1938, **62**, 189.
3 Gaddum, J. H., and Goodwin, L. G., *J. Physiol.*, 1947, **105**, 357.
4 v. Euler, U. S., ibid., 1946, **105**, 26P.
5 *Acta physiol. scand.*, 1948, **16**, 63.
6 *J. Physiol.*, 1939, **96**, 104.
7 Ibid., 1939, **96**, 385.
8 *Amer. J. Med.*, 1948, **5**, 792.
9 *J. Physiol.*, 1946, **105**, 255.
10 McMichael, J., and Sharpey-Schafer, E. P., *Brit. Heart J.*, 1944, **6**, 33.
11 Starr, I., *et al.*, *J. clin. Invest.*, 1937, **16**, 799.
12 Ranges, H. A., and Bradley, S. E., ibid., 1943, **22**, 687.
13 *Klin. Wschr.*, 1948, **26**, 605.
14 *Lancet*, 1949, **1**, 147.
15 *C.R. Acad. Sci., Paris.*, 1880, **91**, 393.
16 *J. Physiol.*, 1935, **83**, 483.
17 *Acta physiol. scand.*, 1948, **15**, 389.
18 Ibid., 1948, **15**, 421.
19 *Nature*, 1949, **163**, 217.
20 *Experientia, Basel*, 1948, **4**, 358.
21 *Klin. Wschr.*, 1948, **26**, 604.
22 *Nature*, 1949, **163**, 363.

for which full returns are available. The number of deaths from diphtheria showed a similar trend: between 1911 and 1940 there had been a fairly steady fall, but the figure appeared to be attaining stability at about 2,500 (2,133 in 1939, 2,480 in 1940, 2,641 in 1941). In 1942, two years after the Ministry's campaign had started, deaths from diphtheria in England and Wales had fallen to 1,827, and the decrease continued: 1,371 in 1943, 934 in 1944, 722 in 1945, 472 in 1946, and 198 in 1947.

Since this remarkable change in the incidence and mortality of diphtheria took place to a large extent during a war in which food shortages, movements of population, and bombing had added greatly to the difficulty of controlling infectious disease, it is clear that A.P.T. possesses the essential feature of a good diphtheria prophylactic—the capacity to reduce to very small proportions the incidence and mortality of diphtheria. Recently, however, some disquiet has been expressed at the variability of A.P.T. as an immunizing agent.[1] Much of this seems to have been due to the use of some preparations of low potency in the 1941 immunization campaign. Though batches of A.P.T. produced by the method of Barr, Glenny, Pope, and Linggood[2] show little variation in antigenic power in guinea-pigs, whether tested by a one- or two-dose method,[3] there is clearly some substance in the contention that the composition of A.P.T. is not accurately known, that it is not reproducible with certainty in different laboratories, and that the amount of carrier (according to Holt,[4] aluminium hydroxide and phosphate) cannot be controlled. There is also some complaint of reactions after A.P.T., particularly in older children and in adults; these are said to be due partly to bacterial protein in the prophylactic. Obviously, therefore, it would be a great advantage to have a diphtheria prophylactic the composition of which was constant and controllable and which caused few reactions—always provided that the immunizing effect was at least as good as that of A.P.T.

These considerations led Mr. L. B. Holt to devise a new prophylactic,[4] and to this he gave the name P.T.A.P. (purified toxoid, aluminium phosphate precipitated). The purified toxoid, produced from the toxin of *C. diphtheriae* grown in a semisynthetic medium, is precipitated by the addition of aluminium phosphate in controlled conditions.[5] By this method toxoid of consistent purity can be adsorbed on known and controllable amounts of aluminium phosphate. The latter point is of considerable importance, since Bousfield[6] has shown that if a constant amount of toxoid is injected as P.T.A.P. the Schick-conversion rate rises with increase in the amount of carrier used. When testing P.T.A.P. by a one-injection method in children Bousfield and his colleagues[7] found that different batches did not vary in antigenic potency, that the Schick-conversion rate by this method was from 94.1% to 100%, and that the antigenicity of P.T.A.P. improves on keeping. Reactions to P.T.A.P. are reported to be trifling in children and in adults, and in individuals sensitive to A.P.T. are less than those caused by the latter prophylactic. (Complete freedom from reaction to diphtheria prophylactics is hardly likely to be achieved: Pappenheimer and Lawrence[8] have shown that some individuals are sensitive to pure diphtheria toxoid.) Nodule formation becomes more obvious as the dose of carrier is increased, and the Schick-conversion rate tends to rise as the incidence and extent of nodule formation become greater.

In this issue of the *Journal* Mr. L. B. Holt and Dr. Guy Bousfield give an account of the present position of P.T.A.P. First, they show that there is no significant difference between batches of P.T.A.P. of the same age as judged by the Schick-conversion rate in children 28 days after a single injection. They also found no difference between the six batches of A.P.T. tested in parallel, but P.T.A.P. did give a significantly higher mean value for the Schick-conversion rate (96.6%, as compared with 87.5% for A.P.T.) 28 days after one injection. They then consider the method of injection, and show that if 5 Lf doses of toxoid are used as antigen in a single dose intramuscular injection gives a higher Schick-conversion rate than subcutaneous injection whatever the quantity of carrier, presumably because muscular movement not only may disperse the antigen but also delays its encapsulation. There is evidence that 5 Lf doses of toxoid adsorbed on 5 mg. aluminium phosphate give the best results. An interesting finding is that even with such small doses of toxoid (15 Lf doses plus 7.5 mg. $AlPO_4$) a Schick-conversion rate of 95% may be obtained three months after a single intramuscular injection. Moreover, even with this small dose the Schick-negative state is maintained in at least 95% of the children for at least 15 months. The authors suggest that these observations indicate that a prophylactic effective against diphtheria by a single injection may be practicable—a matter of obvious importance, since many children never appear for their second injection. At present, however, there are still strong theoretical objections to giving the first course of immunization by a single-dose method. The earlier batches of P.T.A.P. (at *p*H 5) produced some stinging on injection, but it was found that adjustment to *p*H 6.5–7 not only abolished the stinging but made no difference to the antigenicity. From their experience so far Holt and Bousfield recommend a prophylactic containing in 1 ml. 50 Lf doses of toxoid (2,000 Lf doses per mg. protein nitrogen), 10 mg. of $AlPO_4$, 0.85 g. of NaCl, and 0.0001 g. of preservative, adjusted to *p*H 6–6.5 and stored for three to six months in the cold-room before issue.

This work shows what advances have been made in the study of diphtheria prophylactics. There is, however, still a need for caution: the test of a diphtheria prophylactic is its efficiency in the field—its capacity to reduce to a negligible level the incidence of diphtheria and its mortality. Large amounts of bacterial protein in prophylactics undoubtedly increase the frequency and severity of "reactions" after injection; removal of all bacterial protein, though it reduces reactions to a minimum, may reduce the immunizing power even though the Schick-conversion rate is raised. It is therefore exceedingly important that extensive trials of the immunizing power of this new prophylactic should be carried out, preferably over a number of years, in parallel with A.P.T. If the incidence of

1 Bousfield, G., *Publ. Hlth, Lond.*, 1947, **60**, 121.
2 *Lancet*, 1941, **2**, 301.
3 Barr, M., and Glenny, A. T., *ibid.*, 1947, **1**, 385.
4 *Ibid.*, 1947, **1**, 282.
5 Holt, L. B., *Brit. J. exp. Path.*, 1948, **29**, 335.
6 *Lancet*, 1947, **2**, 867.
7 *Med. Offr*, 1948, **80**, 145.
8 *Amer. J. Hyg.*, 1948, **47**, 241.

diphtheria in children injected with P.T.A.P. is as low as, or lower than, the incidence in those injected with A.P.T. then the case for P.T.A.P. will have been conclusively proved.

## AN UNFORTUNATE PRECEDENT

Lord Moran was last week re-elected President of the Royal College of Physicians of London and thus enters his ninth year in this distinguished office. President during a time of storm and stress, he has by his skill in negotiation rendered the profession notable service. Lord Moran has been at the head of affairs longer than any recent presidents, the nearest to him in duration of office being Lord Dawson of Penn, who was P.R.C.P. for seven years. There is, of course, no fixed term of office, the election being annual. But a glance at the history of the College shows that some former presidents had considerable staying power. For example, William Baronsdale (1589–99) and Sir Edward Alston (1655–66) each served for a term of 11 years. Sir Hans Sloane, founder of the British Museum, was President for 16 years, from 1719 to 1735. The president longest in office was Sir Henry Halford, who was elected unanimously every year from 1820 to 1844. He was physician to four sovereigns, and mainly responsible for the removal in 1825 of the College from Warwick Lane to its present habitation in Pall Mall East.

Politics and economics now invade professional life and thought in a way that would have made our ancestors sit uneasily in their chairs of office. Presidents now have to bear a heavy burden and responsibility. As guardians of the gates of ancient and learned institutions they have, Janus-like, to look two ways at once, within and without, at the internal affairs of the Colleges and at the external relations between these and the State. This dual obligation is illustrated by the fact that the present President of the Royal College of Physicians is also the Chairman of the Distinction Awards Committee, a committee which has the difficult—and, as some think, impossible—task of selecting from the body of consultants and specialists in this country those thought fit to receive money prizes. It says much for Lord Moran's strong sense of duty that he has consented to act in these two capacities; and that the Comitia of the College last week re-elected him shows that they do not disapprove of this situation.

The times are exceptional, and exceptional measures and men must be found to match them. Nevertheless we may hope that this is a precedent which will not be followed. Fellows must be able to feel free to criticize the presidents of the Royal Colleges in Council and Comitia, and by fearless advocacy of contrary opinions be able to take part in the needed evolution of these institutions. Those with great expectations for a prize may at times feel constrained to remain silent when it is a question of voicing an opinion thought to be unacceptable to a president who also holds the chairmanship of the Distinction Awards Committee. And, human nature being what it is, some may even be tempted to handle the base coin of adulation. A president's first duty is to promote the interests of his own College, and at times he may, not unnaturally, be unconsciously biased in favour of his own Fellows when it comes to choosing for a prize one or two out of several candidates of almost equal merit. It is true that there is the safeguard of a strong committee and the most careful assessment of claims from the periphery. We have no doubt that the strictest fairness will be observed. Yet many people think that the presidents of the Royal Colleges should not be placed in an invidious position. It may be questioned whether they should serve even as members of the Distinction Awards Committee. It is not impossible that in future the decisions of this committee will be challenged, and it would seem to be important that the presidents of the Royal Colleges should remain free to criticize these decisions, and not be involved in them. The principle, we think, is important enough to deserve careful consideration.

## CONGENITAL HEART DISEASE: A NEW APPROACH

The surgical treatment of congenital heart disease has been one of the most remarkable developments in recent years. In cyanotic heart disease, including Fallot's tetralogy, the Blalock–Taussig operation has proved of great value. The object is to provide an anastomosis between a systemic artery and a pulmonary vessel so that a proportion of the systemic "blue" blood can be shunted into the lung and there oxygenated. In the standard Blalock operation a subclavian artery is joined by an end-to-side anastomosis to the corresponding main pulmonary trunk, while in Potts's operation a side-to-side opening is constructed between the aorta and left pulmonary artery. In addition to these operations there have been successful attempts, including that described by Brock[1] in this *Journal* some months ago, to divide or excise a stenosed pulmonary valve and thereby to increase the blood flow from the heart into the lung.[2]

In the operation in which an anastomosis is to be performed it is essential that the vessels concerned should be large enough for the making of a satisfactory junction; unfortunately in a number of patients with cyanotic disease one or other pulmonary artery may be so small that such an operation becomes impracticable. In these cases the body itself makes an effort to improve pulmonary oxygenation by establishing numerous fine collateral channels in the region of the lung root, and the importance of these may be gauged by the fact that if they are divided and there is no adequate pulmonary artery death may result. Elsewhere in this issue Mr. N. R. Barrett and Dr. Raymond Daley describe a method of treating the cases in which pulmonary arteries are too small for anastomosis by establishing new vascular channels along adhesions between the mediastinum and lung. The adhesions are made by stripping the parietal pleura from the upper part of the chest, then powdering the raw surface with asbestos dust, and re-expanding the lung. This can be done on both sides, and it seems probable that considerable revascularization over the raw area may occur. As an alternative method, omentum has been brought up from the abdomen and applied to lung, since it is known that vascular adhesions can also be established in this manner. Barrett and Daley have treated six patients by one or other of these methods, and they consider that the results were good in two cases and that there was clinical improvement in three. It is too early as yet to say whether the improvement will be permanent.

This form of operation may well be valuable in the treatment of patients in whom the more generally accepted

[1] *British Medical Journal*, 1948, 1, 1121.
[2] Sellors, T. H., *Lancet*, 1948, 1, 988.

type of anastomotic operation is not possible, but at the same time modern methods of investigation must be employed in order to obtain before operation as much information as possible about the condition of the vessels. There are many variations of Fallot's tetralogy and other cyanotic conditions, and no hard-and-fast decision about the type of operation can be made until the chest is opened and the exact abnormality defined.

## TOXOPLASMOSIS

Although the toxoplasma was known to be a parasite in certain animals as long ago as 1908,[1 2] it was not until 1939 that toxoplasmosis was reported in a human patient, the case having been first diagnosed as encephalitozoic encephalomyelitis.[3] Interest in the condition led to a careful review of some earlier case reports and in some cases to re-examination of necropsy material. As a result toxoplasma infection has been suggested as the cause of some previously obscure conditions; among these was a case of "coloboma of the macula lutea in a microphthalmic eye, with parasites in the retina" reported by Janku[4] in Prague in 1923. Since 1939 several authors[5-10] have reported cases of this infection, and recently Jacoby and Sagorin[11] have described the first case of congenital toxoplasmosis diagnosed in this country.

The first cases of toxoplasma infections to be recognized were in newborn babies, but later the condition was diagnosed in older children and adults. While in the latter the signs and symptoms may be diverse (pneumonia, fever, exanthema, gastro-enteritis), in children the usual clinical picture is that of meningo-encephalomyelitis, almost always accompanied by affections of the eye—the most frequent being bilateral chorioretinitis in the central area of the fundus. In a series of 15 cases identified by Wolf and his colleagues[12] as toxoplasmosis, 11 patients were examined ophthalmologically and of these 10 had chorioretinitis. Most lesions were in the healed state and took the form of atrophic pigmented areas resembling macular colobomata. In another report Wolf and his colleagues[8] give the following criteria as typical of toxoplasmosis in infants: (1) onset very early in life; (2) symptoms of meningo-encephalomyelitis; (3) affections of the eye (especially chorioretinitis); and (4) cerebral calcification noticeable on radiographs of the skull. A certain diagnosis depends on the finding of the protozoon by biopsy or necropsy, either directly or after passage through animals. According to Binkhorst[13] this had been accomplished in 18 cases up to 1945, 13 being congenital and five acquired infections. In the case reported by Jacoby and Sagorin the protozoon was not isolated, but neutralizing antibodies were found in the mother's serum.

While ocular disorders such as pupillary abnormality and paresis of ocular muscles have been described in cases of encephalitis, chorioretinitis has seldom been reported as a complication. Its discovery, therefore, in a case of encephalitis of unknown origin should at any rate bring the possibility of toxoplasmosis to mind, especially if cerebral calcification is present. The same would apply if central chorioretinitis was found in a mentally defective child or in a child with Little's disease. The first report in the European literature of a case in which the diagnosis was confirmed *intra vitam* by the demonstration of toxoplasma-like parasites in animals inoculated with the cerebrospinal fluid came from Binkhorst in 1946.[10] The patient was a 6-years-old girl who had been brought to hospital for treatment of a convergent squint. It was noticed that she stumbled when walking, had a copious flow of saliva, and a marked impediment of speech when she endeavoured to talk, which was seldom. Her stature was slight, and she had general motor weakness. Nothing abnormal was found in the lungs, the blood, or the cerebrospinal fluid. Microphthalmus and chorioretinitis were present, and radiographs of the skull in the bi-temporal and fronto-occipital planes showed multiple small and large opacities, with the density of calcium shadows, situated intracerebrally. Micro-organisms resembling toxoplasma were found in a cerebral granuloma in a guinea-pig after the intracerebral injection of cerebrospinal fluid from this case.

Infections of domestic animals in this country have not hitherto been reported, but Jacoby and Sagorin mention that a dog in Kent was recently found to have toxoplasmic encephalitis, the diagnosis being confirmed by identification of the protozoon. Toxoplasmosis in human beings may be more common than is thought, and it should be considered as a possible cause of visual disability in children in whom no direct interference with the light path is immediately noticeable.

1 Nicolle, C., and Manceau, L., *C.R. Acad. Sci., Paris*, 1908, **147**, 763.
2 Splendore, A., *Rev. Soc. sci. S. Paulo*, 1908, **3**, 109.
3 Wolf, A., Cowen, D., Paige, B. H., *Amer. J. Path.*, 1939, **15**, 657.
4 *Cas. Lek. ces.*, 1923, **62**, 1021.
5 Pinkerton, H., and Weinman, D., *Arch. Path.*, 1940, **30**, 374.
6 —— and Henderson, R. G., *J. Amer. med. Ass.*, 1941, **116**, 807.
7 Sabin, A. B., ibid., 1941, **116**, 801.
8 Wolf, A., Cowen, D., Paige, B. H., *Arch. Neurol. Psychiat.*, 1942, **48**, 689.
9 Zuelzer, W. W., *Arch. Path.*, 1944, **38**, 1.
10 Binkhorst, C. D., *Ophthalmologica, Basel*, 1946, **113**, 239.
11 *Lancet*, 1948, **2**, 926.
12 *Arch. Ophthal., Chicago*, 1943, **29**, 1.
13 *Ophthalmologica, Basel*, 1948, **115**, 65.

## BRITISH HOSPITALS ASSOCIATION

Voluntary hospitals having passed into history, it was inevitable, though none the less to be regretted, that the British Hospitals Association should follow them. The association, which is now being wound up, can look back upon a fine record of service extending over 65 years. Its end is in no sense due to any failure or shortcomings of its own. It is a political casualty, and the voluntary hospitals, whose interests the association so effectively represented, have now been taken over as a going concern, continuing their service into the new era of regional administration.

The British Hospitals Association was formed to focus the views of hospitals under voluntary management, and with the help of a very large council, representative of hospitals all over the country, it brought them to the attention of Government Departments and public bodies generally. Its patron was the Duke of Gloucester, and its president for not far short of 30 years was the late Sir Arthur Stanley, who had a lifelong enthusiasm for all hospital causes. The association also owed much to the wise guidance of its chairman, Sir Bernard Docker. It had 25 area committees in England and Wales, a branch in Scotland with five committees, and a branch in Northern Ireland. The task it undertook was a difficult one. Voluntary hospitals were always highly individualistic institutions, proud of their traditions and jealous of their area of local or special appeal. It was no small matter to get them to combine for a common purpose, even for such a thing as the adoption of a uniform system of accountancy or statistics. In all the work connected with hospital financing and development of recent years, such as the growth of contributory and provident schemes, organized collections, the training of almoners, dietitians, and administrators, the association has exercised a useful influence. Under its auspices, together with the Joint Council of the Order of St. John and the British Red Cross Society and other bodies, there was established a Central Bureau of Hospital Information,

which has been responsible since about 1930 for the compilation of the *Hospitals Year Book*, incorporating *Burdett's Hospitals and Charities*, founded in 1889. This annual publication, alike as a directory, a financial review, and a statistical record, has made itself indispensable to all concerned with hospital administration, voluntary or municipal.

Early in the planning which led up to the National Health Service the British Hospitals Association put forward its own views. It recognized the value of a system of regional hospital councils, each council with its medical advisory committee, being set up as statutory bodies and charged with the duty of planning in detail for the hospital, consultant, and specialist service in their areas. It saw no difficulty in the continuance of two hospital systems side by side, with equal representation on the regional councils. The voluntary hospitals had never set out to establish a comprehensive service for the whole nation, and the association was fully aware of the enormous scope for local authority effort in the field of hospital provision. At the same time it urged that as the voluntary hospitals had accumulated a long tradition and experience, while local authority enterprise in this field was of comparatively recent origin, the voluntary hospitals might well form a touchstone against which the efficiency of the newer service could be judged. That was in 1944. Events have moved swiftly since then, and one of the unfortunate results is that, the voluntary hospitals having lost their voluntary status, the British Hospitals Association can no longer exercise its representative function on their behalf.

## SAFETY IN CARS

In the aircraft industry physiologists and engineers have co-operated to design apparatus to eject pilots from the cockpits of high-speed aircraft and to reduce the effects of over-violent acceleration, whether in turning or pulling out of a dive. Another safety measure is the fitting of shock absorbers strong enough to take the strain of a bad landing even by a heavy aircraft. But, according to Woodward,[1] in automobile engineering "the only influence of aircraft design apparently so far adopted . . . is the erroneous one that the aerodynamic principles of a jet-propelled aircraft should be applied to a vehicle the speed of which should be limited to 55 miles per hour on the ground." Taken by itself there might appear to be an element of the dogmatic in the speed limit proposed. But in an inquiry conducted by the Safety Department of the American Automobile Association, out of 4,102 replies received four drivers favoured the introduction of governors limiting top speeds for every three which opposed such a device; and the highest speed favoured by the supporters of governors was 55 m.p.h. This, however, is only one factor and not perhaps the most important: for, though speed was found to be a contributory cause in two out of five fatal accidents, the proportion of accidents in which the speed had exceeded 50 m.p.h. was only one in five.

Woodward suggests that physiological and psychological principles should now be applied in automobile design in the same way as they have already been successfully applied in the case of aircraft. If all-round vision is important, then front supporting columns should be moved to the rear. If low windows lead to fractured elbows due to "side swipe"—a suggestion supported by radiographs—then windows should be higher. On the other hand, they should be wide enough to serve if necessary as emergency exits, and perhaps it is for this reason that Woodward prefers a single door to two doors on each side. It might, however, be thought that two doors on each side would offer an improved chance of escape if one or more of the doors jammed as a result of an accident. To prevent front seats crashing forward in emergency stoppages and increasing the impact of knees or legs on dashboard would seem to be an elementary precaution. It would also be wise to include on speedometers an indication of the stopping distance appropriate to the speed of travel. It is not easy to provide a good view of the roadway from a "streamlined" car, and in the inquiry already referred to only one in six of American drivers voted for appearance as an important factor in body design. Some of us may feel impelled to cut a dash, in appearance as well as speed, when we take the road. If the American inquiry is anything to go by both qualities could be dispensed with without user protest provided that the more important quality of acceleration was retained. No doubt safer cars could be designed, and it would be interesting to see how far a campaign for a safe car, as opposed to one which looked and performed like a speed-track monster, could be commercially successful.

[1] *J. Amer. med. Ass.*, 1948, **138**, 627.

## TREATMENT OF GONOCOCCAL VULVOVAGINITIS

The treatment of gonococcal vulvovaginitis before the introduction of the sulphonamides and penicillin was very unsatisfactory; it was always a prolonged process and often taxed the ingenuity of the most experienced practitioner. Relapse was all too common, and in some cases cure was delayed till the vaginal epithelium had changed its character from that of the infant to that of the adolescent. Even the sulphonamides were by no means always effective, and sulphonamide resistance was not unusual: whether this was due to resistant strains of bacteria or lack of reaction on the part of the host was often not clear. With the advent of penicillin the whole picture changed; a few injections of the drug in aqueous solution cured most patients, and even orally administered penicillin was often successful. Clarke and Eisenberg[1] treated 20 girls aged 2–10 years with a single intramuscular injection of 100,000 or 200,000 units of penicillin in oil–wax and obtained lasting cure in all but one case. The failure was in a girl most probably reinfected about four months after apparent cure, and she was finally cured by a second injection. Unless penicillin-resistant strains of gonococci develop—and up to the present there is no suggestion that they have—the outlook for controlling this previously intractable condition is bright. Moreover, much of the danger of cross-infection, so much feared in the past in residential nurseries and other institutions for young girls, will have gone, since infected children can now be rendered non-contagious in a matter of days or even hours.

[1] *Amer. J. Dis. Child.*, 1947, **74**, 707.

The Moynihan Lecture will be given in the Riley-Smith Hall of the University Union in Leeds on Monday, April 25, at 3 p.m., by Professor G. Grey Turner, Emeritus Professor of Surgery in the University of London. His subject will be "Moynihan and the Training for Surgery."

Dr. N. Hamilton Fairley, F.R.C.P., F.R.S., will deliver the Croonian Lectures before the Royal College of Physicians of London (Pall Mall East, S.W.) on Tuesday and Thursday, May 3 and 5, at 5 p.m. His subject is "Malaria, with Special Reference to Recent Experimental Clinical and Chemotherapeutic Investigations."

# A REGIONAL ORTHOPAEDIC AND ACCIDENT SERVICE

BY

G. R. GIRDLESTONE, D.M., F.R.C.S.

A few months ago this *Journal* (Oct. 23, 1948, p. 751) approved a short publication of mine on the organization of a Regional Orthopaedic and Accident Service within the National Health Service, and asked for further information. I am now trying to answer the questions; but as that article was written a year ago, when we knew very little about regional machinery, it is best to include a brief general review.

## An Outline of the Service

A comprehensive orthopaedic and accident service should cover: (*a*) Acute diseases affecting the locomotor system, together with accidents of all kinds. These conditions require a 24-hour service in all the area hospitals of the region, best run in each such hospital under an orthopaedic and accident surgeon who lives in its vicinity. While the great majority of accidents involve the locomotor system, there may be damage to eye, brain, thorax, abdomen, etc.: thus the man in charge often requires the expert assistance of his colleagues in other branches of surgery. (*b*) The multiplicity of cases of congenital or acquired deformity, insidious disease, and so on, which may be termed the "cold" orthopaedics of the scattered clinics and the orthopaedic hospital.

There may be one or several orthopaedic hospitals in a region. In the Oxford region there are two—the Manfield, at Northampton, and the Wingfield-Morris, at Oxford. My illustrations are taken from the latter, for which I have worked in a regional service for nearly 30 years.

In order to understand and appreciate the organization of a modern orthopaedic service the reader should bear in mind from the beginning two rather special considerations which are easily overlooked. The first is the necessity for widely scattered out-patient facilities for diagnosis and treatment. In "cold" orthopaedics children form a majority of the patients, and in this work *very early discovery, prompt effective treatment,* and *prolonged aftercare* are the three fundamental conditions of success. Now, a mother finds great difficulty in taking her child to a distant hospital; indeed, she will seldom do so unless the doctor's advice is reinforced by the child's obvious need. Thus the lack of a clinic within easy reach may be very harmful. If an early diagnosis is to be made the patient should be seen by an experienced specialist long before anything serious or painful is evident, and if cure is to be assured attendance must be kept up long after the success of treatment is apparent (and to the mother fully satisfying). For these reasons clinics within easy reach of every village in the region are regularly attended by the staff of the central orthopaedic hospital. In these neighbourly clinics early diagnosis is achieved much more often than would otherwise be possible, and the prolonged periodic follow-up which so many orthopaedic cases require is facilitated. This is no theoretical statement, but the outcome of ample experience.

Though many of these clinics are held in hospitals they are, taken together, the out-patient department of the central orthopaedic hospital, extended for the benefit of its distant patients. For three reasons it is essential that members of the senior surgical staff should visit the clinics: first, because very early diagnosis of major conditions is a matter demanding considerable experience and judgment; secondly, because the achievement of a full correction of these innumerable minor cases demands much co-operation from the parents, which can seldom be achieved without the authority and influence of a senior specialist; and, thirdly, because prolonged follow-up is far better carried out by a senior man who attends the clinic continuously year after year.

The second consideration concerns "cold" orthopaedics—a slow-moving complex field of work, in which sound judgment grows very slowly with experience and much failure and frustration, or fairly quickly and without failure and frustration by membership of a team of men, seniors and juniors, with all the opportunities of guidance and discussion that this gives. It is characteristic of "cold" orthopaedics that a surgeon is often unable to distinguish between the ultimate success or failure of his treatment, or to assess the relative value of different methods of treatment, until years have passed. Furthermore, the great variety of disorders of the locomotor system afford a dangerously wide scope for invention: indeed, much ingenuity has been exercised in many centres for many years, with results varying from beneficial to disastrous. This is a potent reason for the frequent demonstration, examination, and free discussion of cases which will save the younger men from trying over again methods which appear excellent but have proved unsound. At the Wingfield the whole staff meets twice a week, spending about an hour and a half on the examination (in one room) and discussion (in another) of five or six patients, new and old. This is the soundest possible source of learning.

A regional orthopaedic and accident service can be organized on the following pattern.

## A. Central Orthopaedic Hospital

The whole organization is built round the central orthopaedic hospital, which in a regional centre is likely to form the clinical field of the medical school. It is probably better that it should be under the Regional Hospital Board than be regarded as part of the teaching hospital, and that it should have its own individual board of management. There may be more than one first-class orthopaedic hospital in a region, each the centre of its own regional organization.

These hospitals have a number of special characteristics: (*a*) wards designed for treatment in open air and sunshine; (*b*) theatres with every possible means of promoting asepsis and, preferably, a Plenum system of filtered-air ventilation; (*c*) plaster-rooms with much special equipment; (*d*) first-class radiographic and photographic departments; (*e*) physiotherapy with treatment baths for anterior poliomyelitis and much other special equipment, and staffed by experts; (*f*) occupational therapy; (*g*) school teachers for the education of children of school age (2–16) grouped suitably by ages in wards; (*h*) workshops equipped and staffed for the quick and exact manufacture and fitting of splints, and research into new designs and new material.

*Hospital Records.*—That clinical records should be full and accurate is of particular importance in an orthopaedic hospital because many of its patients are under treatment from time to time over many years, and without explicit and reliable records the progress, whether improvement or deterioration, may be impossible to assess with any accuracy. Here the visual records of photographs "before and after" and of small individual "before and after" loops of cinematograph film are of extraordinary value; for by these demonstrative and realistic means the surgeon is made fully aware of the effects, good or bad, of his treatment.

*Research.*—The opportunities for clinical research are many, the need is great—perhaps especially for more exact knowledge on the relative value of different methods of treatment, based on written, radiographic, photographic, and cinephoto records before and after. Each orthopaedic hospital ought to keep such records and make accurate assessment of its end-results in complete series of cases. It would find the material wholesome for its own consumption; and it could thus contribute to the general knowledge of orthopaedics. It is desirable that members of the surgical staff should be given an opportunity of taking part in animal research in university laboratories.

*Library.*—There should be a good medical library, with facilities for reading, writing, and dictation for all members of the staff.

*Pathology.*—For regional work the clinical pathology is carried out in laboratories under the supervision of the senior clinical pathologist of the teaching hospital. This seems preferable to a completely independent system of laboratories.

## B. Regional Staff—Central Orthopaedic Hospital

*Director of Orthopaedic Services.*—The clinical administration of the Regional Orthopaedic Service within the central orthopaedic hospital and throughout the region is best entrusted to one of the surgeons, who will of course work in the closest

touch with his colleagues as a member of the Staff Committee. Much of his work is clinical administration; some of it is clerical, to co-ordinate and facilitate the working of the organization. Most of his decisions are made after full discussion with the Staff Committee; particularly will this be so when something has to be done to improve an unsatisfactory service. If he should turn out to be too much of a "director" he can be replaced. The post should not itself carry any extra emolument; so that if a change of directorship should be desirable it may be made without financial disturbance.

*Regional Consultants.*—Several of the senior surgeons of the central orthopaedic hospital should be recognized as regional consultants and be responsible for the orthopaedic departments in the area hospitals. Each of these men will visit one or more such hospitals every week. Here he will have the assistance of the local orthopaedic and accident surgeon, and they should work intimately together in the wards, theatre, and out-patient department.

*Specialist Surgeons.*—A number of surgeons who have not yet reached regional consultant rank complete the surgical staff of the central orthopaedic hospital, which should provide about one surgeon to every 50 beds. The work of the staff covers the intramural work of the central orthopaedic hospital, the orthopaedic and accident departments of the central and area general hospitals, and the outlying clinics.

*Professor of Orthopaedic Surgery.*—Where the regional hospital is closely associated with a teaching hospital its staff may include a professor of orthopaedic surgery, who, with his first assistant, can be given charge of one of the units of the hospital. He thus plays his part in the regional work of the hospital. He is responsible to the university for the organization and carrying out of all academic activities throughout the hospital. In an article so general as this it is hardly possible to specify the relations between the regional director, with his widespread administrative and co-ordinating duties, and the professor, with his academic interests. Much will depend on individual circumstances. Their functions should always be mutually helpful.

The establishment of resident staff is as follows. At the central orthopaedic hospital, with, say, five surgical units: one resident of senior registrar status and five house-surgeons of junior registrar status. At each of the area hospitals with accident and orthopaedic departments the services of a man of senior registrar status and a house-surgeon are required.

### C. Area Hospitals

In the area hospitals—i.e., the principal general hospitals of the region—there are (1) the orthopaedic department, mainly for out-patient service, but with some beds for short-stay cases; and (2) the accident service.

The staffing of these outlying units is of particular concern. The orthopaedic and accident work should be closely co-ordinated. It is essential that the surgeon in charge of the service should be a member of the regional orthopaedic team. The best arrangement is that the visiting regional orthopaedic consultant who is responsible for the orthopaedic department of the area hospital should also be consultant to its accident service and be prepared to see difficult cases and discuss problems with the accident surgeon, and that the latter, in turn, should work in the orthopaedic department as assistant surgeon (to use the old term), and be on the staff of the central orthopaedic hospital. For these outlying posts it is possible to pick from a strong field of candidates a man with sound experience of the accident side of orthopaedics, with a Fellowship, and with a background of sound surgical training. But for the most part, when appointed, he has not had very much experience of "cold" orthopaedics.

Nevertheless these men are from the first active and valuable members of the orthopaedic staff of the region, not only taking care of orthopaedic emergencies (their primary service), but also helping the visiting consultant to cope with the flood of "cold" orthopaedics which comes to an area hospital. Their value in this field will increase as they accept the opportunities of absorbing orthopaedics from their association with the central orthopaedic hospital. Whenever possible, they take part in the clinical conferences at that hospital as a member of its staff and on sessional duty. Even if the pressure of work makes some of these visits to the centre impracticable they have the advantage of close association with an orthopaedic specialist who has been working in that intensive school for years. Thus, for example, in the southern part of the Oxford region there is in view a staff of five whole-time surgeons living at the centre, with four men working in and living near the area hospitals.

There is a tendency to speak of major and minor orthopaedic cases and to set up a distinction between them in regard to their need of specialist skill—let us say between the lesions of the spine and the larger joints and those of the hand or foot. This is a mistake. The smaller tasks are often the more delicate and intricate, requiring as much judgment and more exact technique—and what happens to his hand or foot is of major, not minor, importance to the patient. But many of these short-stay cases make no special demands on hospital design and equipment, and therefore need not be admitted to the central orthopaedic hospital.

### D. Outlying Clinics

A certain number of *ad hoc* orthopaedic clinics in the smaller towns have been found necessary, in addition to the orthopaedic out-patient clinics of the general hospital, in order to bring the means of specialist diagnosis, treatment, and after-care within the easy reach of patients, particularly children, in every part of the region.

### E. Proportion of Beds to Population

It is probable, judging from our own experience at the Wingfield, that about 300 beds per million population are sufficient, provided that the beds in the central orthopaedic hospital are supplemented by provision of a total of 40 or 50 beds for short cases in the associated general hospitals. Orthopaedic hospitals do, however, differ considerably in regard to the type of cases they admit. In the Wingfield we have always had a considerable proportion of active orthopaedics—i.e., acute inflammation or injury of any part of the locomotor system—a good many cases of difficult fractures, non-unions, mal-unions, and so on, and internal derangement of joints. On the other hand, by a very closely knit system of orthopaedic clinics we are able to allow patients to leave hospital very much earlier than is otherwise possible. Almost all our patients go home a few days after first getting out of bed.

### F. Aftercare Sisters—Orthopaedic Physiotherapists

These are highly trained girls who have obtained a certificate in orthopaedic nursing, are members of the Chartered Society of Physiotherapy, and have had a postgraduate training in the great variety of plaster and splint work used in orthopaedics. This triple training makes them invaluable in out-patient orthopaedic work of every kind, as well as in the plaster-room of the central and area hospitals. Their responsibilities and duties have hitherto been primarily those of working for the orthopaedic surgeons in the plaster-rooms of the central orthopaedic hospital, in the out-patient departments of the area hospitals, and in the outlying clinics. But they have carried in addition the responsibility of attending the outlying clinics weekly between the surgeon's periodic visits and carrying on treatment by remedial exercises, plaster work, and the supervision of splintage. Their remedial exercise work is largely class-work, made effective by their capacity to impress upon the mothers of the children the importance of keeping up these exercises and maintaining good posture during the intervening period. This is simple and economical, and can be a most effective way of getting rid of postural defects, with far less interference with school-time than is necessitated by the regular attendance of children at the hospital or clinic for daily remedial exercises. It is noteworthy that, at a census taken in 1927, of 540 children under treatment at clinics in Berks, Bucks and Oxon, 509 were attending school.

The number of children attending the clinics is, of course, only a small proportion, probably a very small fraction, of the number who need remedial exercises. Here we see the immense advantage of close liaison between the orthopaedic personnel and the School Medical Service, with organizers of remedial exercises associated with that Service. This association is

valuable both in regard to the supervision of the right sort of exercises in schools by the School Service and in promoting the recognition of those types of deformity which call for the attendance of the child at an orthopaedic clinic for diagnosis and treatment.

Our staff numbers five fully trained members and one undergoing postgraduate training. They live in the neighbourhood of the central orthopaedic hospital. Their time is divided in about equal proportions between work in the central orthopaedic hospital and the outside hospitals and clinics.

### Three Important Questions

Three questions remain to be answered—those of cases of acute anterior poliomyelitis, combined pulmonary and skeletal tuberculosis, and workshops.

*Acute Anterior Poliomyelitis.*—In general, cases of acute anterior poliomyelitis can be admitted and isolated in the central orthopaedic hospital as soon as they can safely be moved. It is probable that more can be done to minimize the severity of paralysis during the first three weeks than at any subsequent stage. In a time of epidemic, however, there is likely to be too great a rush of cases for this immediate admission and isolation to be practicable; therefore a sufficient number of beds in an isolation hospital within easy reach of the central orthopaedic hospital should be allocated to meet this need, and the patients placed under the joint care of the isolation medical and nursing staff on the one hand and the orthopaedic surgeons and aftercare sisters on the other. Where such ready co-operation can be promoted the effect is admirable. As the patients pass out of quarantine they can be admitted to the orthopaedic hospital.

*Combined Pulmonary and Skeletal Tuberculosis.*—Pulmonary tuberculosis is best treated in a sanatorium, and skeletal tuberculosis is best treated in an orthopaedic hospital where the surgeon and his resident staff devote their whole time to the study and care of the locomotor system, and where constant practice makes the nurses capable of ensuring the comfortable, effective, and long-continued immobilization of a hip or a spine on a frame or in plaster. It is recommended that a special unit should be developed for this work in every region, as convenient as possible for the physicians and surgeons concerned. Experienced nurses, prepared for long-term service, are necessary, for only thus can their patients be given comfort and confidence through a lengthy period of confinement which is always difficult and can be very distressing.

*Workshops.*—I can best answer this question by saying that our Wingfield workshops have been fulfilling the needs of the Wingfield Hospital and its clinics, together with some work, mainly but not exclusively orthopaedic, for the Radcliffe Infirmary, Oxford, the Royal Berkshire Hospital, Reading, the Royal Buckinghamshire Hospital, Aylesbury, the R.A.F. Hospital at Halton, and the Ministry of Pensions Hospital at Stoke Mandeville. It is probable that this workshop staff and equipment could serve a regional orthopaedic and accident service for a population of at least a million. Our staff and space consist of :

| | |
|---|---|
| Superintendent .. .. | Office, 68 sq. ft. (6.3 sq. m.) |
| Clerks (2) .. .. | General office, 220 sq. ft. (20.4 sq. m.) |
| Boot repair dept. (9) .. | 680 sq. ft. (63 sq. m.) |
| Machine shop (6) .. | (including one blacksmith) machine shop, 864 sq. ft. (80 sq. m.); forge, 130 sq. ft. (12 sq. m.); welding, 81 sq. ft. (7.5 sq. m.) |
| Carpenter's shop (1) .. | 490 sq. ft. (45.5 sq. m.) |
| Saddlers (3) .. .. | 432 sq. ft. (40 sq. m.) |
| Stores .. .. .. | 306 sq. ft. (28.4 sq. m.) |
| Fitting-room .. .. | 180 sq. ft. (16.7 sq. m.) |
| Waiting-room .. .. | 54 sq. ft. (5 sq. m.) |
| Dispatch-room .. .. | 80 sq. ft. (7.4 sq. m.) |

### Conclusions

A Regional Orthopaedic and Accident Service can render a high standard of service if the personnel is first-rate and works as a team in a well-planned and complete organization. The orthopaedic and accident services should be closely articulated in those parts of the region where they are not fused. In the area hospitals a local orthopaedic and accident surgeon is in immediate charge of the work as a member of the regional team. The orthopaedic service is directed from the central orthopaedic hospital, with an out-patient department in every hospital and in sufficient additional clinics to bring a consultant frequently within reasonable reach of every village in the region. This arrangement and other extramural organization are necessary to bring about early diagnosis, regular attendance, and thorough follow-up. The efficiency of treatment depends on the ability, spirit, and character of the members of the team; for in truth much of the clinic work will prove tedious to the staff, and largely ineffective to the patient, unless it is tackled with obvious and infectious interest. Though organization can facilitate their attendance, patients will keep coming only if they understand what is being done for them and why it must go on so long.

Orthopaedic work must be very good or it is marred by frequent failure and much disappointment. It demands a great deal of skill and effort from all concerned, and particularly is this true of "cold" orthopaedics, for in this field there is often a strong tendency towards recurrence of deformity, with as much harm as help from *vis medicatrix naturae*.

My work for the E.M.S. in two regions during the war made me acutely aware of the needless suffering that was being endured and the disablement that was being promoted in reputable hospitals as a result of members of their surgical staff treating fractures in an atmosphere of isolation and seclusion. For example, I found a young soldier who had suffered a compound fracture of the femur a few days before, in great pain and distress. His lower limb was tightly bandaged to a long Liston splint, the upper part of which was completely free in the bed and some distance from the trunk. The fracture was uncontrolled and in obvious varus deformity, and I was told that the splint was detached daily for dressings.

Regional Hospital Boards have indeed grave responsibility—and great opportunity. They can put an end to a long epoch of isolation and seclusion in which the work of individual surgeons all over the country has been good, bad, or indifferent. Isolation bred incompetence, seclusion hid it, and no one could do anything about it.

Each Board must aim at a sound organization, staffed by a team of men who share their advance in knowledge and clinical experience, a team who will thus come to be distinguished by the diffusion of a high standard of skill and a spirit of wholehearted service. In order to achieve such a team there must be some devolution of authority step by step from the Director of Orthopaedic Services right through his senior and junior colleagues, the resident staff, and all the personnel of ancillary departments and clinics. Since the team is animated by a common purpose this authority can be exercised almost entirely by the guidance and personal influence of the senior men. When, however, a man continues to prove himself unable to render first-class service his appointment must be terminated by the Board.

The regional organization on which this article is based has been tried over many years, and has earned the approval of local authorities, voluntary hospitals, and all concerned. How far it can be applied to other specialties I do not know—probably only in some of its features. It seems likely that a considerable number of autonomous areas will be required for medicine, for surgery, and for gynaecology. No doubt, too, a pattern which suits the country as a whole will be modified for the service of industrial areas with great density of population.

In many regions local associations for the care of cripples will be found; these are voluntary bodies capable of giving most valuable help to the secretaries, almoners, and surgeons of orthopaedic hospitals.

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The American people are contributing funds to finance a campaign against heart disease. The American Heart Association is seeking five million dollars to carry out research, to spread information about the disease, and to provide community services for its victims. President Truman has urged that the utmost support of governmental and voluntary organizations be given, and said recently, "Combating the nation's leading cause of death has become our most serious national health problem."

# TRAINING OF NURSES

## NURSES' BILL

The Nurses' Bill, which is sponsored by the Minister of Health, was given a first reading in the House of Lords on April 12. The Bill is intended to improve the training of nurses, and its provisions follow closely some of the recommendations of the report of the Working Party.[1] This report[2] criticized the present constitution of the General Nursing Council which was first set up[3] under the Nurses Registration Act of 1919. It urged, for example, that elections to the Nursing Council should be by hospital regions. The report also proposed the reorganization of the present methods of training nurses. These proposals, which we commented on in a leading article,[4] have now been put before Parliament in the form of this Bill, of which the full title is "An Act to reconstitute the General Nursing Council for England and Wales and otherwise to amend the Nurses Acts, 1919 to 1945, and to make further provision with respect to the training of nurses for the sick."

### Reconstitution of General Nursing Council

The proposed new Council will consist of 34 members, of whom 17 are to be elected by nurses, 12 appointed by the Minister of Health, three by the Minister of Education, and two by the Privy Council. Of the elected members, one will be drawn from each of fourteen areas designated by the Minister. There will also be special representation for mental nurses, sick children's nurses (by election), public health nurses, sister tutors, ward sisters, and male nurses (by appointment).

A Mental Nurses Committee of the General Nursing Council will consist of six members of the Council (including two mental nurse members), two elected mental nurses, and four persons appointed by the Minister—a matron, a mental nurse tutor, "a doctor teaching psychiatry," and a chief male nurse. Matters mainly concerning mental nurses other than questions of registration or removal from the *Register* will be referred to this committee.

If this Bill is enacted the General Nursing Council will not be able to refuse approval, or to withdraw approval, from a training institution without giving the managing body written notice and an opportunity to be heard. Appeals against such refusal or the withdrawal of approval will be heard by a person nominated by the Lord Chancellor, instead of being made to the Minister of Health. The General Nursing Council will be empowered to admit to the *Register* nurses trained anywhere abroad to a standard considered by the Council to be satisfactory, or, if below that standard, after such further training as the Council may direct. This proposal will replace the provisions of the 1919 Act, which restricted such admission to the *Register* to those Dominions that granted reciprocal treatment to British nurses.

Male nurses, who are at present only admitted to a special supplementary part of the *Register*, will in future be admitted to the general part of the *Register*. A minor but important change is that the General Nursing Council will be empowered to charge nurses already registered or enrolled fees for life registration or enrolment. These fees will take the place of the present annual retention fees. The General Nursing Council will no longer be under an obligation to publish the *Register* but will publish periodical lists of admissions and removals.

### Proposals for Training

The Minister will be given power under this Bill to constitute by order standing nurse-training committees for each of the fourteen hospital areas in England and Wales. The members of these committees will be representative of regional hospital boards, boards of governors, the General Nursing Council, the Central Midwives Board, local health authorities, local education authorities, and universities. Among the duties of these committees will be the promotion of improvements in nurse-training and research into methods of training; advice and assistance to training institutions in preparing and carrying out training schemes; and advice and assistance to the General Nursing Council on the approval of training institutions.

These regional nurse-training committees, which are very much as envisaged by the Working Party, will also allocate among the training institutions the money provided by the Exchequer through the General Nursing Council for training. By this means the finance of nurse-training will so far as practicable be independent of the finance of hospital administration. Experimental schemes of training which are not in accordance with the rules in force at the time may be adopted by these committees subject to the approval of the General Nursing Council.

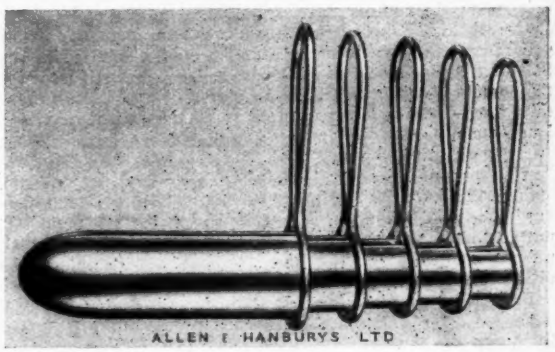
One of the last clauses in the Bill empowers the Council to pay to its members and to members of the Assistant Nurses Committee sums in respect of the loss of remunerative time as well as travelling and subsistence expenses. The Bill, which is a short one of 19 clauses and three schedules, will have the effect of repealing many of the provisions of the Nurses Registration Act, 1919, and the Nurses Act, 1943.

[1] *Report of the Working Party on the Recruitment and Training of Nurses*, 1947. H.M.S.O. 2s. 6d.
[2] *British Medical Journal*, 1947, **2**, 426.
[3] Ibid., 1920, **1**, 616.
[4] Ibid., 1947, **2**, 422.

# Preparations and Appliances

## VAGINAL DILATORS

W. MCKIM H. MCCULLAGH, F.R.C.S., F.R.C.O.G., senior obstetric surgeon, City of London Maternity Hospital, writes: The standard glass vaginal dilators are readily broken and occasionally an undiscovered crack causes their disintegration in the vagina, with difficulty in removing the fragments. In addition, the glass dilators have no handles, and, as half of those patients requiring their use have psychological inhibitions in regard to the entry of anything into their vagina, it is important that their phobias be considered and that the instruments used be as little fearsome as possible. Handles inserted at right angles to the penis replica assist in instructing the patient in the location and direction of her vaginal passage, which is an important factor in curing dyspareunia and assisting coitus. The upper and anterior surface of the dilator is grooved, to lessen pressure on the urethra.




One is surprised at finding not a few long-married patients each year still *virgines intactae* and others ignorant of the fact that a happy marriage necessitates painless complete physical union. I find these new forms of dilators here illustrated of great assistance in treating such cases, and especially so in vaginismus cases, where even after dilatation of the vagina by operation the introduction of a small dilator causes vaginal spasm. Personal attention by the surgeon is psychologically necessary, and these safe dilators give extra confidence and extra mechanical knowledge to the patient when introduced day by day in order of size, after operation, till a sufficiently large one is employed.

The metal dilators are hollow, and are supplied in nests by Allen & Hanburys, of Wigmore Street, W.1, and the Coldlite sets are supplied by Vann Bros., of Weymouth Street, W.1.

During the first quarter of this year 276 children were admitted to Dr. Barnardo's Homes. The number of children rescued from destitution by these Homes in March was 114.

# Correspondence

## Diabetic Coma

SIR,—I have read with great interest Dr. J. G. H. Sheppard's account (April 2, p. 576) of a case of diabetic coma treated with 56,000 units of insulin, and congratulate him on both his courage and its reward. In view, however, of the great potential dangers associated with the use of active insulin in such heroic dosage I would like to ask whether a control test for potency was carried out on the insulin used in this case.

It is important to remember that the giving of 56,000 units of insulin does not prove that this dose was necessary or, in view of the severe delayed hypoglycaemic reactions described, even desirable. It seems probable that in the very severe type of case described by Dr. Sheppard a large proportion of the insulin given in the resistant phase is destroyed before it has time to act, and I know of no convincing evidence that the amount of insulin utilized can be increased by increasing the dose above a certain optimum level. Experience would suggest that this level is far below the dose given by Dr. Sheppard. No mention is made of the volume of fluid administered intravenously, and the persistence of a very high pulse rate suggests the possibility that more rapid clinical improvement might have resulted from more intensive treatment of the dehydration.

I find it difficult to believe that the sudden collapse was due to the accidental substitution of 5% glucose for normal saline in the drip, especially in view of the controlled observations on the mode of action in diabetic coma of saline and glucose respectively published by Drs. J. Lee, D. Naidoo, and J. A. Torrens in the same issue (p. 565). Incidentally, in the article referred to, the authors correctly include the name of Dr. R. D. Lawrence among those who "administer glucose as a beneficial procedure" in diabetic coma, but I would like to point out that in the department of which he is the director it has been the custom for the past ten years to give normal saline for the first three hours of treatment of cases in diabetic coma.—I am, etc.,

London, S.E.5. WILFRID OAKLEY.

SIR,—Professor H. P. Himsworth (April 9, p. 632) considers our glucose-treated and saline-treated cases (April 2, p. 565) not comparable because he feels that the age levels, the alkali reserve, and the blood-pressure readings can be interpreted differently.

First, with regard to the age, the mean for group A is 35.9 (standard error of mean ±5.15, standard deviation 16.3) and for group B 33.3 (S.E. of M ±3.74, S.D. 15.9). These are comparable. It is true that mortality rises with age, but there can be no justification for making a special choice of 50 years, which taken by itself can give little information about the duration and severity of the diabetic process and the degree of its detrimental effect on the cardiovascular-renal and nervous systems. Had Professor Himsworth chosen 40 as his necessarily arbitrary critical age he would have been faced with 9 cases in the saline series and only 3 in the glucose series, producing the very opposite impression. Nevertheless, the over-50's in the saline cases did not die.

Secondly, the errors inherent in the estimation of the alkali reserve at such low figures make the alleged difference of 2.2 vol. $CO_2$ per 100 ml. between 9.8 vol. and 12 vol. meaningless. But this difference is only the result of Professor Himsworth's arithmetic. In fact, the actual averages for the fatal cases in each group are 9.8 vol. and 9.5 vol.—very similar figures. Joslin (*Diabetes Mellitus*, 1940, 7th ed., London, p. 388) says that "among *unconscious* patients the percentage of deaths was essentially the same in the group with $CO_2$ values above 10 vol. as with the group with low values." No single factor is all important, and even in a combination of factors each will assume a different relative importance. We have used Collen's index, which is not an absolute standard, but as it is equally applied to both series it is governed by no more logic than a yard-stick.

Thirdly, the average systolic and diastolic blood pressures in each group are comparable. Any special selection on the basis of an arbitrary figure can be of little value. A consideration of the diastolic pressures might equally be taken to indicate that the fatal saline cases were more serious than the fatal glucose cases.

We do not wish to claim that our contention is "mathematically significant," because for this purpose we should have required almost twice the number of cases. Over fifty cases treated under strictly similar conditions would have been impossible to collect in a period which included the final months of the war, with its attendant nursing difficulties, and which saw the introduction of penicillin. Our poorly documented wartime cases which were treated with glucose but were not included in the series because of the special difficulties encountered in their management bear out the mortality figures given for the group A cases. Group B cases now total 20 with 2 deaths.

We agree emphatically with Professor Himsworth that glucose is a potent weapon for the correction of disordered carbohydrate metabolism, that the depleted electrolytes should be supplied, and that the rapid fall in plasma potassium and phosphorus may lead to serious symptoms.

We wish to point out that although it was not possible to provide a sufficient number of cases for strict mathematical proof our cases provided evidence that the administration of glucose to seriously dehydrated cases of diabetic coma in the *early* stages of treatment increases the water output, interferes with rehydration, worsens the state of circulatory collapse, and in some cases may indeed precipitate death.—We are, etc.,

J. LEE.
D. NAIDOO.
J. A. TORRENS.

Isleworth, Middlesex.

SIR,—Drs. J. Lee, D. Naidoo, and J. A. Torrens (April 2, p. 565) have endeavoured to demonstrate that the administration of glucose to serious cases of diabetic coma in the early stages of treatment "increases the mortality significantly." For this purpose they took 28 comparable cases and found that, using glucose, 10 cases suffered a 40% mortality, whilst 18 cases, using saline, suffered an 11% mortality. They have then "proved" their point.

However, if we examine their results statistically it can be shown that these two series of cases have a standard error of 16.2%. The difference between the percentage mortalities (40% − 11% = 29%) is less than twice the standard error, and it is generally accepted that this difference might easily have arisen by chance and is not significant. The series of cases quoted is much too small to justify the authors' claims.—I am, etc.,

London, W.9. C. A. ROYDE.

SIR,—I quite agree with Drs. J. Lee, D. Naidoo, and J. A. Torrens (April 2, p. 565) in the conclusions of their valuable contribution to the question whether or not to use glucose as a preliminary measure in treating diabetic coma. Although the comparison is somewhat difficult because of a slight difference in the age of both groups, this difference is more marked by the lower figures of the alkali reserve in group A, the glucose-treated cases. The common feature in the fatal cases of both groups is the very low alkali reserve (with one exception 10 or under 10 vol. $CO_2$ per 100 ml.). Though the Collen index is equal in both groups, this index takes no account of the depletion of the $CO_2$ reserve—a most important factor in assessing the severity of the case and the chances of recovery. If the $CO_2$ reserve is very low and does not improve markedly within the first 4–8 hours, the chance of recovery is poor. It is, therefore, more important to give an alkali intravenously as a preliminary measure. The absorption by the stomach is often very much impaired in diabetic coma, and any solutions given are either vomited or found many hours later in a greatly dilated stomach, as proved at necropsy.

The importance of the alkali reserve in the treatment of diabetic coma has been pointed out by Professor H. P. Himsworth (April 9, p. 632), who refers to the recent investigations by Butler and his colleagues.—I am, etc.,

Wembley, Middlesex. S. P. BARTFELD.

## The Intervertebral Disk

SIR,—The *Journal* of Feb. 12 has three contributions that illustrate the increasing importance of the intervertebral disk.

(1) When a stooping man begins to extend his spine, says Sir H. E. Griffiths (p. 255), the posterior margin of the disk is compressed between the posterior margins of the vertebral bodies.

*Comment.*—This could happen only if the vertebral body pivoted on the disk, as the tibia pivots on the talus. The vertebral bodies, in fact, move apart during extension of the joints, which are situated three centimetres behind the posterior margins of the bodies; pressure on the disk is therefore reduced.

(2) Perforation of the annulus fibrosus by a spinal needle is followed by seepage of the nucleus pulposus through the hole (Dr. C. Langton Hewer, p. 283).

(3) When pain in the leg follows septic infection of the lumbar canal we are required to believe ("Any Questions?" p. 292) that the disk must have been injured during a supposedly ill-performed lumbar puncture.

*Comment.*—The annulus fibrosus must disobey the rules of healing that are observed by all other tissues. Puncture even of an artery—whose contents are fluid and under high pressure—does not lead to escape of its contents. The nucleus, too, must be unlike all other tissues: it is fluid enough to seep out through a tiny puncture in a ligament and at the same time solid enough to interrupt nerve roots by pressure.

In order to make possible behaviour that is without parallel in biology, the quality of "turgor"—self-expansibility—is often attributed to the nucleus. But "to ascribe turgor or power of expansion to the nucleus is to invoke some property quite unknown in the physical world and takes medicine back to the obscurantism of the Middle Ages. . . . If the volume of a fluid increases, something must have been added to it from without; if it decreases, part of its substance must have been removed."[1]

The disk is nothing but a resilient bit of fibrocartilage, more cartilaginous in its centre and more fibrous at its margins. It cushions sudden or intermittent pressure by flattening and it is restored to its previous shape when the compressing force is removed. Its resilience is shown by the rarity of disk lesions in compression fractures of vertebral bodies. It is rarely seen as a whole because of its inaccessibility, and—on the principle *omne ignotum pro magnifico*—fairy tales have been invented about it that can be disproved only by the expenditure of much labour. We are a credulous profession and often prefer the incomprehensible to the simple explanation.

In other parts of the body pain that appears during muscular effort is due to strain of muscles or ligaments. In many cases of back strain the same cause can be demonstrated by local analgesia. Yet the recent fashion demands that we invoke a complicated mechanism whose reality cannot be proved, that makes of the vertebrochondral relationship a ball-and-socket joint, and that takes away from the pedicles and articular processes their historic function of weight-bearing.

We take advantage of this weight-bearing function when we allow a patient with a crush fracture to walk about with his spine in extension. Narrowing of an intervertebral space is always secondary to failure of the weight-bearing structures through decalcification, with sagging and sometimes the appearance of linear stress fractures.[2] The disk, which is not constructed to bear continuous pressure, accommodates itself by flattening. Narrowing of the space, therefore, is not the cause of the pain but a later effect of the decalcifying process.—I am, etc.,

Melbourne, Australia. MICHAEL KELLY.

REFERENCES

[1] Roberts, Ff., *Brit. J. Radiol.*, 1944, **17**, 54.
[2] Roberts, R. A., *Chronic Structural Low Backache*, 1947, London.

## Bronchography and Surface Analgesia

SIR,—Mr. R. C. Brock (March 12, p. 454) strongly condemns bronchography by direct tracheal puncture. He favours the use of an indirect method in which the iodized oil is trickled into the glottis from the nose or pharynx, and he argues that direct puncture is unnecessarily dangerous, more complicated, and gives no better results than the indirect method. Nevertheless, after trying both techniques, we are convinced that tracheal puncture is a safe procedure and that it has definite advantages over the indirect methods.

In the past our experience on the resident staff of the Brompton Hospital covered a period of thirteen years, during which time we saw almost all the bronchograms performed there. These amounted to over 10,000, the large majority of which were done by direct puncture. The only serious complications were four cases of cellulitis of the neck; all these occurred in patients with large amounts of heavily infected sputum, which we now regard as a contraindication to the use of this method. All recovered satisfactorily, although they occurred before the days of chemotherapy.

Direct puncture requires a little more apparatus than the indirect method, but in our opinion the superior results more than compensate for this. The method itself is easy to master with proper tuition, and its speed commends it to both doctor and patient. Our criterion of a good bronchogram is that every segmental branch of the appropriate bronchial tree shall be outlined. There is always an element of luck in bronchography, and it is impossible to guarantee one hundred per cent success with any method. Nevertheless, after long experience we are convinced that tracheal puncture produces a higher percentage of good bronchograms, particularly of the upper lobes, than the indirect transglottic methods. The direct puncture technique has the great advantage that the patient can be placed in the appropriate position for outlining each lobe before the oil is introduced.

Properly performed, tracheal puncture is painless, and patients who have had experience of both methods often prefer it because it is quicker. We have done bronchograms by direct puncture under local anaesthesia on intelligent children as young as six years without causing them any distress.

We agree with Mr. Brock that the cricothyroid membrane is best avoided; the needle should be inserted into the trachea just below the cricoid cartilage. A few minims of procaine are sufficient to anaesthetize the skin, and we agree that many patients will tolerate the introduction of the iodized oil without further anaesthesia. But a few will not, and it is not possible to pick these out beforehand. One good cough can ruin a bronchogram, and therefore we inject 0.5 to 1 ml. of 2% "butyn" into the lumen of the trachea as a routine measure. Tracheal puncture should not be used if the patient has large quantities of fetid sputum, and in such a case an indirect transglottic method is preferable.—We are, etc.,

G. S. TODD,
King Edward VII Sanatorium, Midhurst.
A. F. FOSTER-CARTER,
Brompton Hospital Sanatorium, Frimley.

## Penicillin-resistant Staphylococci

SIR,—Drs. A. Voureka and W. Howard Hughes (March 5, p. 395) state that they identified 315 distinct strains of staphylococci obtained from 241 patients on the basis of colonial appearance, haemolysis, and coagulase production. I find this difficult to believe, and thought that such nice distinction could only be obtained by phage-typing. I should be glad if anyone could confirm that such results are possible. Staphylococci are of major importance in Saskatchewan and constitute an important part of the work in bacteriology in Regina. Since phage-typing is not readily available it is important to know if such distinction in typing can be achieved by the naked eye. For myself, I think not.—I am, etc.,

Regina, Saskatchewan. N. G. B. MCLETCHIE.

## Adoption

SIR,—The Adoption Bill is evidently intended both to facilitate desirable adoptions and to safeguard children from being placed out unsuitably; it may be hoped that in its ultimate form, after the incorporation of desirable amendments, it will do both more effectively.

It starts with the statement (Section 1 (1)) that a child may be adopted by his mother with or without her husband, or by his natural father with or without his wife. Adoptions of a child by his mother and her husband are already frequent, and no doubt the great majority of legal adoptions by a child's own mother, which were stated in the debate in the House

to be a third of the whole number, are by her and her husband together. Those who come professionally into contact with mothers in difficult circumstances can sometimes help them to take heart about the future by emphasizing to them and their relatives the truth that a man who marries a woman who already has a child often wishes to bring up her child as though he were his own, and can with her legally adopt the child and so give him his mother's new married name. It is not true that a mother who rises to her responsibility for her own child is less likely to marry happily in the future than if she gives her child away; on the contrary, a happy marriage is much more likely to be founded on candour and responsibility accepted than on secrecy and responsibility evaded.

Adoptions by a mother and her husband also include some where a married woman has given birth since her marriage to a child by another man. Such a child already has a claim to his mother's married surname even without adoption by her husband, and his birth certificate, if the new short form is used (available since 1935 in Scotland and 1947 in England) need not reveal any irregularity. Therefore a husband who is prepared to accept his wife's child out of mercy towards him or love of his mother may not feel any necessity to adopt him legally, but it is perfectly competent for him to do so with his wife, and the point of Section 1 (1) is not to make this legal but to call attention to the fact that it is legal already. Knowledge that it is possible may come as a great relief to a husband who wishes to express in action his reconciliation with his wife and good will to her child.

This Bill will be valuable if it stimulates adoption by a child's own kindred, but no legislation is needed to stimulate offers of adoption by strangers. Would-be adopters who appear suitable at first sight already exceed in number the suitable children available. There is accordingly never any need to jump at the first offer of adoption that presents itself, and Section 5 of the Bill is apparently designed to lessen the risk of over-hasty or unsuitable adoptions.

Negotiations for the adoption of a child into the family of strangers should not be entered into before he is born or without the sponsorship of a registered adoption society or local authority, for the following reasons:

1. No final judgment that a child is suitable for adoption can be made until he is born and has been carefully tested and observed. The placing of children who prove physically or mentally unsuitable causes very great disappointment and difficulty.

2. The decision whether a particular offer from would-be adopters should be encouraged should be made by a body which receives many offers and is in a position to select. The paramount consideration should always be the welfare of the child, and *no adoption should be promoted for its possible therapeutic effects on the adopters*. The wise bringing up of an adopted child calls for great integrity of character and stability of purpose, especially during the strains of adolescence.

3. A mother should not be encouraged to consent to the proposed adoption of her child under any duress of circumstance or family pressure, or to arrive at a final decision while she is still pregnant or before she has fully recovered from her confinement. It is not until her child is born that many a mother understands the strength of her own love for him, and she may afterwards bitterly regret and resent a separation from her child which she had previously seemed to desire. Parenthood, even unmarried parenthood, brings privileges as well as burdens, and to remove a child from his mother is not only to relieve her of a burden, it is to rob her of a privilege and maybe to inflict a wound on the integrity of her nature.

Where circumstances seem at first sight too difficult to permit a mother's bringing up of her own child, the National Council for the Unmarried Mother and her Child, 21, Coram Street, London, W.C.1, or the Scottish Council for the Unmarried Mother and her Child, 17, Wester Coates Avenue, Edinburgh, 12, should be consulted. Through these bodies and the local societies working with them many mothers of all social types and degrees of education are helped to rise to the responsibility and some measure of the privilege of their motherhood. Sometimes, though much less often than the inexperienced might suppose, the adoption of the child is the right ultimate solution, but always with proper safeguards and never in a hurry.—I am, etc.,

ANNE ASHLEY,
General Secretary,
Edinburgh Council of Social Service

Edinburgh.

## Physiological Basis of Vagotomy

SIR,—Mr. A. Davis Beattie (April 9, p. 607) attempts to justify vagotomy as a physiological procedure for the treatment of peptic ulcer by relying on the neurogenic elements of its aetiology. He admits, however, that ulcer may occur both in the asthenic and sthenic types, and rejects the inborn diathesis in favour of a psychosomatic type with parasympathetic preponderance brought about by nervous stress. He refers to the work of McCrea and his associates, who emphasize that there is no true antagonism between the vagus and the sympathetic nerves. McCrea[1] states:

"Each nerve is undoubtedly both efferent and afferent, transmitting centrifugal and centripetal impulses, and concerned with motor, vasomotor, secretory, and sensory functions of the organ. . . . The cutting out of one system of regulators (therefore) gradually results in the diminution and in almost a disappearance of control by the remaining system, the final results approaching but not attaining the effects of section of both. In this complete denervation, the intrinsic automatic mechanism takes on the proper functioning of the stomach no longer guided by external reflexes."

McCrea points out that the disorders of gastric function may be produced by either hypo- or hyperfunction of the extrinsic nerves, and that the primary cause which gives rise to such disorders may be located (1) peripherally, (2) in the nerve paths, or (3) centrally. To take these in reverse order: disorders of central origin may be constitutional, as suggested by Eppinger and Hess, and are possibly a result of endocrine instability; there is no evidence that they ever result in peptic ulcer formation. Disorders of the nerve paths are obviously too rare to be taken into serious consideration. The peripheral irritation, according to McCrea, is the most common cause, and is the result of inflammation which he rightly interprets as the pre-ulcerative stage.

This inflammation cannot be produced by the secretory response of vagal stimulation since acid by itself cannot produce the ulcer; and Beattie recalls that Dragstedt has shown that peristaltic activity and gastric secretion alone are not sufficient to delay physiological healing. It cannot be too strongly emphasized that the cause which is responsible for the local inflammation (which starts in the mucous membrane) is also responsible for the initiation of the ulcer and the maintenance of its chronicity.

In which way then, may it be asked, does vagal section arrest the progress of this morbid process, and what mechanism will be available to record whatever may go wrong in the stomach, since its immediate effect is the abolition of pain? It is difficult to follow the argument that by severing the stomach from its vagal control it can be claimed that there is "physiological basis for vagotomy."—I am, etc.,

J.-JACQUES SPIRA.

London, W.1.

REFERENCE

1 *Brit. J. Surg.*, 1926, **13**, 621.

## Artificial Insemination

SIR,—In his letter (April 2, p. 590) Dr. Robert Forbes again refers to the Archbishop of Canterbury's Commission on Artificial Insemination. This was a mixed body of clergy and laymen—among the latter lawyers—whose sole dissentient from findings otherwise unanimous and unacceptable to Dr. Forbes was one of the clergy, the Dean of St. Paul's. He further ignores that the whole Commission, including the Dean, had nothing to say against artificial insemination by the husband's semen. This is not fair controversy.

All systems of jurisprudence have admitted the existence of two systems of law: one called the Divine, or God's, or natural; the other that of the realm or State. Apart from any theory as to the origin of the former, a court of the latter can and will on due occasion hold that what may or may not be right or admissible in the latter is contrary to the natural rights of the person or persons concerned and therefore inadmissible.

Whatever system of natural or Divine law any system of jurisprudence admits, it ordinarily holds that law is unalterable, and all that remains is to ascertain what it is. The proper persons to enunciate what on any particular point it lays down are clearly those concerned principally with the system in question; and in this country the division which arose about four centuries ago between the clerical and the legal professions

leaves the clergy with the duty concerned. Once the Divine law on any particular matter is known it is open to the different States of the world to leave their individual systems in accord or discord with it, or to bring them into accord or discord, as the State chooses. The risk of a divided loyalty on the part of its subjects, who in the last resort, all experience shows, will obey the law of God rather than the law of man, is wittingly run by the State which chooses discord.

In the debate in the House of Lords to which Dr. Forbes refers it appeared common ground that artificial insemination by a donor's semen constitutes adultery until doubt was thrown upon this view by, I believe, Lord Merriman. This is also the view of the Archbishop's Commission with the exception of the Dean of St. Paul's. Adultery in some systems of State law has been both a criminal and a civil offence (that is, an offence against the State and also against the offended spouse); in others, among them our own, it is a civil offence, the remedy being divorce, but no criminal penalty attaching. But in every system of Divine law adultery has in one way or another been regarded as sinful. The Greeks, whom we revere as the fathers of medicine, worshipped (practically as well as by offering and oblation upon her altars) a goddess of fornication whom they admitted had no power over the goddess of the home and who was at constant enmity with the goddess of the marriage bed and of childbirth in wedlock.

It is therefore incorrect to say that the doctor in attendance alone can determine whether A.I.D. is fitting and proper. He is no more entitled than anyone else to transgress either the Divine or the secular law. No matter how many legal precautions may be advised by Dr. Forbes or used by the practitioner, either he is doing right or he is doing wrong; and with exceptions only of individuals on certain relatively minor points all who have examined this subject consider he is doing wrong to advise or execute it. Answerably it is incorrect to say the law may require alteration. The Divine law can neither require nor receive alteration: it is laid down for ever. Our secular law on this matter appears in substance to be in accord with the Divine law; and if Dr. Forbes and his associates procure a deviation they are by so much further extending that discord between the Divine law and the law of the country already mentioned as a source of danger through the imposition of a divided loyalty.—I am, etc.,

London, S.W.6. C. T. NORRIS.

SIR,—Whether Lord Merriman was right or wrong in describing as worthless the document approved by the Medical Defence Union for use by the parties concerned in A.I.D., his opinion coincides with that of the eminent legal experts who advised the Archbishop of Canterbury.[1] They state (p. 40) that the "assurance suggested by the Medical Defence Union as proper to be obtained by the doctor—that the birth of a child will not defeat the claims of any person to any titles, estates, interests, or funds—is one that could never be properly given or accepted."

This, however, is a matter that only the lawyers can settle. It is otherwise with the ethical aspects of A.I.D. Dr. Robert Forbes asserts (April 2, p. 590) that the "decision whether artificial insemination will constitute appropriate treatment for any given patient rests within the judgment of the doctor in attendance. He and he alone can determine whether or not it is fitting. . . ." But this is to beg the very question at issue: it is, in the last resort, society as a whole that must decide whether or not it is "fitting." Few can doubt that serious moral considerations are involved. Yet Dr. Forbes upbraids the Church for making its views plain before A.I.D. has been "properly examined by competent authorities and either condemned or confirmed." Who these authorities are and by what standards they are to "condemn" or "confirm" Dr. Forbes does not say. But to condemn the Church for forming its own judgment, after taking into account all the available evidence—medical, social, legal, and psychological—is surely illogical. If the Church is not a "competent authority" in such a matter as this, with the right to declare its views, will Dr. Forbes tell us why?—I am, etc.,

Redhill, Surrey. G. L. RUSSELL.

REFERENCE

1 *Artificial Insemination*, 1948. London: S.P.C.K. See also *British Medical Journal*, 1948, **2**, 523.

## Painless Childbirth

SIR,—The subjects of painless childbirth and analgesia are very much in the forefront at present in the Press and in parliamentary circles. Varying opinions have been expressed as to the relative merits of different agents and whether it is advisable to allow midwives to be equipped with "trilene" inhalers.

I should like to express my appreciation of the Minnitt gas-air apparatus, which is the one in use most frequently at present. This apparatus, designed by Dr. Minnitt, does just what is claimed for it. It provides a safe and suitable method of analgesia for use by midwives when no doctor is present.

According to the Central Midwives Board regulations, the midwife must be accompanied by an assistant when analgesia is to be administered. The most important part of the midwife's duty is the delivery of the baby, and a method of analgesia which had a definite risk to the mother would demand too much of her attention at a critical point in the conduct of the case. With the exception of the small percentage of non-cooperative patients, the rule is to find that patients express appreciation of the relief afforded by this method of analgesia. Transport difficulties seem to be the stumbling block, since the apparatus is somewhat heavy to carry.

There are two attachments for use with the Minnitt apparatus which enhance its analgesic effect and still keep the apparatus within the limits of safety. One is the Chassar Moir attachment, which allows the patient to have a few breaths of pure nitrous oxide followed by the 50% gas-air mixture. This initial nitrous oxide deepens the analgesic effect at the right point, and yet recovery from it is rapid. This method is very suitable for the time when, as a rule, inhalation analgesia is commenced—that is, towards the end of the first stage. There is a sufficient interval between pains for the reservoir bag to refill.

The other supplementary method is the Rowbotham bottle with a Walton fitting, into which 6 dr. (21 ml.) of trilene is placed. This method was demonstrated to me by Dr. Minnitt and I have used it in a considerable number of cases. In the second stage, and for delivery, the gas-air mixture is diverted over the surface of the trilene and affords marked relief.

Midwives receive a very comprehensive and excellent training, and a high standard of proficiency is demanded from them at the end of it. Analgesia is now included in the curriculum. The two supplementary methods I have mentioned for use with the Minnitt apparatus could be included in the category of safe and suitable methods for the trained midwife.

From my experience of observing their work in hospital I should say that they are very careful when using analgesia and tend towards under- rather than overdosage. They could have a somewhat wider range than at present to help them in conducting the normal midwifery which is their province. I do not think that they would abuse the privilege or that any harm would come to the mother or infant.—I am, etc.,

Bearsden, Glasgow. ELLEN COWAN.

## Psychiatric Indications for Abortion

SIR,—The annotation (March 19, p. 489) entitled "Psychiatric Indications for Abortion," arising from changes in Swiss law, is of great interest. I hope I may be permitted to comment upon certain points.

1. Where pregnancy is the result of rape, the fact of rape does not in itself constitute a reason for termination. The mental strain consequent upon the birth of a child so conceived must, however, be a potent factor in determining the post-natal condition of the mother's psychic, and therefore also her physical, health. That this view is admissible under English law was upheld by Mr. Justice Macnaghten in the Bourne case (reported in the *Journal* of July 23, 1938, p. 199). Considered in this sense the Swiss law does not seem dissimilar.

2. It is very hard for a socialized State to admit that economic grounds for termination can exist. Here again, however, under even the best social safeguards very great inequalities must always continue. As your annotation rightly points out, no system of family allowances and maternity benefits can be adequate for the over-prolific family. The income which is reasonable for the average family, providing not only shelter, clothing, and food but the opportunity of rest and convalescence for the mother, will not be enough to secure the same benefits as the mother with repeated pregnancies—whose need is none the less the greater.

3. When the question of defining admissible psychiatric grounds is raised, we are upon even more uncertain terrain. As Dr. Ellis Stungo (April 2, p. 590) very sensibly points out, each case must be considered upon its merits. Those "merits" cannot be judged only from the patient as a "body," or even as a "mind," without consideration of the total picture.

How did the act of conception come about? In what sense is the mother, married or unmarried, emotionally involved with the father? Is the mother, if unmarried or deserted, on good terms with her parents, or has she friends who can accept the situation? Will the emotional trauma likely in many cases to follow thwarted motherhood have greater repercussions in the long run than the immediate difficulties leading to the request for termination? These are some of the questions which must be faced. In order to face them the doctors concerned cannot be too fully informed regarding every aspect of the background. This is where the "family doctor" can be invaluable and by his information and advice has it in his power to contribute enormously to the prevention of much misery.

4. Where a patient is in so disturbed a mental condition as to warrant continual watching for the prevention of suicide, that in itself would seem to be strong evidence of such severe mental conflict as may lead to complete breakdown. I would, however, like to put on record my disagreement with Dr. Stungo that in doubtful cases it is always wiser not to resort to termination, but to endeavour to reconcile the expectant mother with the reality factors of her situation. In genuinely doubtful cases I consider it wiser to give the mother the benefit of the doubt.

I should like to conclude by asking you, Sir, whether it might not be appropriate for medical men throughout the country to seek the establishment of a Royal Commission to investigate and, if possible, to suggest amendments of the law concerning termination of pregnancy. There can be few doctors, and even members of the general public, who do not feel it an anomaly that pregnancies, the result of positively illegal acts—e.g., rape or seduction of a girl below the age of consent—cannot be terminated, if the demand is made, *upon that ground alone*. Similar considerations would seem to apply in the case of insane patients desirous of termination, and in those instances where congenital syphilis or a long-standing family history of insanity make it reasonably certain that the offspring will be tainted—with consequent serious repercussions upon the mother, the child, and the community as a whole.

It would also protect doctors and safeguard the general well-being of the mothers of the nation if at the same time the whole question of psychiatric indications for abortion could be submitted to public examination with suggested positive reforms in law.—I am, etc.,

London, W.1. EUSTACE CHESSER.

## POINTS FROM LETTERS

### Prescription of Barbiturates

Dr. NATHAN FINN (Johannesburg) writes: Dr. H. H. Margulies (Feb. 19, p. 325) in his constructive criticism of my communication (Jan. 29, p. 195) exaggerated the emetic dose of pulv. ipecac. In my experience many people complain of nausea even after ½ gr. (5.4 mg.), and many actually vomit from such a dose. In my humble opinion, shared perhaps by others, there is some contradiction in the arguments put forward by Dr. Margulies, who does not tell us if his statements were made from observations on patients. Theoretically he may be right, but every theory must be proved, otherwise it just remains a theory utterly useless to a practitioner. The question is one of great practical importance. The solution cannot be to stop prescribing a so well-established and also most useful preparation. In my experience "ersatz" preparations are far from satisfactory.

### Irreducible Umbilical Hernia in Pregnancy

Dr. MARGARET M. NOLAN (Anua, S. Nigeria) writes: On July 16, 1948, an Anang woman of the Calabar Province, aged about 26, was admitted to the antenatal ward. She was 5 months pregnant and was complaining of much pain in the umbilical region. On examination she was found to have a medium umbilical hernia which was tender but apparently reducible. On Aug. 2 she complained of no bowel movement for 24 hours, and she had much abdominal pain; the hernia was now irreducible. After an injection of "omnopon" ¼ gr. (22 mg.) and under local infiltration with "nupercaine," the hernial sac was isolated and removed with a portion of adhering gangrenous omentum. The hernia was repaired according to the Mayo technique, chromic catgut No. 0 being used. The wound healed by first intention. The pregnancy continued to term, the patient having a normal delivery of a living female infant weighing 6¼ lb. (2.8 kg.) on Jan. 2, 1949. The puerperium was normal, and the patient went home on the tenth day.

# Obituary

## JOHN W. BONE, LL.D., M.B., C.M.

Dr. John W. Bone, whose record of service for the British Medical Association was outstanding, died at his home in Luton on April 14 at the age of 79. He had been treasurer for nine difficult years, and for thirteen years before that he had been chairman of the Medico-Political Committee, which afterwards became the General Practice Committee.

John Wardle Bone was born in 1869, and in 1891 he graduated M.B., C.M. with first-class honours at the University of Edinburgh. Four years later he took the B.Sc. in public health. After serving in some resident appointments, including one at Clayton Hospital, Wakefield, he settled in general practice at Luton in Bedfordshire. He was kindly and painstaking, and yet the sort of man who would "stand no nonsense," and he had an admirable way with him, particularly in dealing with children. From 1896 onwards he was closely identified with the Luton Children's Hospital, though he did not actually receive a staff appointment there until 1899. In 1905 he became honorary medical superintendent of the hospital, and during his tenure of office he was responsible for various extensions and improvements. He resigned the position of medical superintendent in 1933, while remaining a member of the committee of management and continuing to take a great interest in the hospital. He was also honorary consulting surgeon to the Bute Hospital, Luton, and a co-opted member of the maternity and child-welfare committee of the town council.

Dr. Bone did not become a member of the British Medical Association until 1905, but he quickly made his personality felt in his own Division, of which he was chairman in 1910. He also represented the Bedfordshire and Hertfordshire Division at annual representative meetings from 1911 onwards, and entered the Council in 1920. In 1922 he was president of the South Midland Branch. When the Association was called upon to choose from a number of candidates the two who should have its support at the 1928 election of direct representatives for England on the General Medical Council, Dr. Bone was one of those selected, the other being the late Sir Kaye Le Fleming; both were returned by large majorities. On the General Medical Council he was a very active member and most skilful in the examination of witnesses. Often after counsel on both sides had completed their examination Dr. Bone would rise and with a few questions, asked through the chair, give a quite fresh aspect to the case.

He was not a great platform man, and confessed that he was never happy with the microphone in large assemblies, but he was an ideal member of committees. His tongue was occasionally caustic and his manner dour, and when in the chair he never concealed his impatience at undue protraction of the business. Nevertheless, he had a great sense of fun, and his delight in some quip would often relieve a tedious afternoon. The gradual serpentine movement of committee procedure really interested him; he knew that it was there, and not in larger and more showy gatherings, that the business was done. His work for the British Medical Association in the committee-room, usually at Headquarters but sometimes at the House of Commons or on deputations to Government Departments, was of great value. His own contributions to debate were always persuasive and critical, and he had the capacity for working in a team and throwing his whole weight into a cause.

The list of John Bone's Headquarters activities would run parallel with the medico-political activities of the Association

from 1920 onwards. In addition to his work in the General Practice Committee, which at one time had as many as twenty subcommittees, he had been a member at various times of the Central Ethical Committee, of the committee concerned with certification under the Workmen's Compensation Act, of the committees on Health Services, on Lunacy Law and Mental Disorder, on Medical Education, on Poor Law Reform, and many others. Bone's membership of the Insurance Acts Committee dated from 1923, and there again he served on a bewildering number of subcommittees. A useful piece of work in which he took particular interest was his chairmanship of the committee which put up so effective an opposition to the Osteopaths Registration Bill when it came before the Select Committee of the House of Lords in 1935. On all questions connected with pharmacy and dangerous drugs he was an acknowledged expert. He was a member of the Advisory Committee on the Pharmacy and Poisons Act, known as the Poisons Board, and brought to the work a surprising amount of detailed knowledge. Earlier he had been a member of the watching committee set up by the Association in regard to the revision of the *British Pharmacopoeia*. He was also one of the five members nominated by the Association on the Board of Directors of the British Medical Bureau. Another excellent achievement was his part in the settlement of the dispute at Llanelly, which arose in 1934 between the local profession and the Workmen's Committee. He was one of the three or four representatives of the Association who visited the area and spent three days in hearing evidence and making the fullest possible local inquiries.

Dr. Bone was a man of considerable business sagacity. He succeeded the late Mr. Bishop Harman as Treasurer of the Association, and for nine years showed his mastery of the financial policy of a great organization. His treasurership included the anxious period of the second world war, when important decisions had to be made almost from day to day. He managed to combine, in a way that carried general approval, a firm control of expenditure with a policy of expansion adapted to meet the great demands on the Association which he foresaw as likely to arise in the post-war years. His presentation of the financial report year by year was never seriously criticized. He was also treasurer of the National Insurance Defence Fund, and one of the treasurers of the General Medical Council.

At the Cambridge meeting in 1948, when he retired from the treasurership, the Council unanimously decided to award him the Gold Medal of the Association for his exceptional services—a decision which evoked enthusiastic approval when it was announced to the Annual Representative Meeting. In 1946 Dr. Bone received the Hon. LL.D. of his own University of Edinburgh.

Dr. Alfred Cox writes: For some weeks now Dr. Bone's old friends have been sorrowfully awaiting the inevitable end, but nevertheless it is very sad to think that B.M.A. House will see him no more. For many years, as is well shown by the preceding narrative, he was there nearly every day and there were few of the Association's activities in which he did not take an active part. He was not easy to know intimately. He had the old-fashioned idea that a man's private life was his business, and would have resented intrusions on it. But it was a pleasant revelation to see him at home as I did occasionally when he was in active practice. We had some kindred interests which helped me to get behind the somewhat "dour" Bone. He was a North Countryman and could always be drawn on his early days in the North. He never got rid of his Northumbrian "burr" and never tried. He was a great collector of books, which, unlike some collectors, he read, and he could talk, and talk well, about his favourites. I should put Bone high among the men of business capacity who have served the Association. He was eminently a man of orderly and logical mind and hated waste, though he could always be converted to approval of large expenditure by the Association once he saw its possibilities. This was brought out before he became treasurer in the enthusiastic support he gave to his old friend Sir Robert Bolam when he fathered the ambitious scheme for the extension of B.M.A. House. From what I saw of his methods of practice it did not surprise me to learn that he had built up one of the most successful general practices in the provinces. Bone was no lover of the limelight—nor indeed of those who obviously sought it. But he was sound all through, and no man ever more faithfully earned the Gold Medal of the Association. It is a grief to all his friends that he never received it in due form amidst the applause of all of us who knew him and who would have been delighted to have been able to say to him, "Well done, good and faithful servant."

## DONALD GEORGE HALL, M.D., F.R.C.P.

Dr. Donald Hall died very suddenly at his home in Hove on April 7 from coronary thrombosis at the age of 72. His early years were spent at Gatehouse-of-Fleet, a lovely spot in Kirkcudbrightshire, where was nurtured his intense attachment to his native land. He was educated at the Edinburgh Academy, and from there gained a scholarship in natural science at Emmanuel College, Cambridge, where in 1897 he took a first-class tripos in the same subject. Returning to Edinburgh to complete his medical course, he graduated M.B., B.Ch. in 1900. There followed resident appointments at the Royal Infirmary and the Royal Hospital for Sick Children, Edinburgh, and then, like many a Scot, Hall migrated southwards and became house-physician at the Royal Sussex County Hospital, Brighton. Subsequently he put up his plate in Hove, and thus began a general practice which was later to bring him such a well-deserved reputation.

In 1903 Hall proceeded M.D., and in the following year he was elected assistant physician to the Royal Sussex County Hospital. Soon after the 1914–18 war he began to make a special study of the treatment of pulmonary tuberculosis by artificial pneumothorax, and of the use of the electrocardiograph. He became a recognized authority on both subjects, and his election in 1945 as chairman of the Cardiac Society of Great Britain and Ireland was a tribute to his profound knowledge of the diseases of the heart. Dr. Hall was elected F.R.C.P. in 1923 and thenceforth confined himself to consulting practice. He was the trusted adviser of an ever-widening circle of doctors and their patients, and the esteem in which he was held was reflected in the frequency with which his colleagues called upon his help in their own illnesses and those of their families.

Donald Hall was an able physician and consultant. Kindly and inspiring confidence, he had a remarkable memory which enhanced the value of his wide experience, his incisive mind, and a sure clinical instinct. His opinion and advice were equally clear and decided, and whenever possible he offered a reassuring and optimistic outlook to the patient. When the chairmanship of the Royal Sussex County Hospital became vacant in 1938, Hall, though still an active member of the honorary staff, was unanimously elected to this important and onerous post. He filled it with conspicuous success for eight years, and it was largely due to his wise guidance that the hospital was able to fulfil its many obligations during the difficult years of the recent war. In 1946 his services to the hospital were recognized by his appointment as its president. Hall was president of the Brighton and Sussex Medico-Chirurgical Society in 1927, chairman of the Brighton Division of the B.M.A. in 1926–7 and again in 1931–2, and president of the Sussex Branch in 1933–4. In the Boer War he had served on the hospital ship *Nubia*, and in the 1914–18 war in the Second Eastern Hospital, with the rank of major. In his younger days he captained his college rugby team, and later played forward for the famous Edinburgh Academical side, which included several internationals. Hall was a good shot and a keen fisherman. For many years he spent his holidays shooting and fishing in Scotland or Northumberland with his friends. Many will remember his and Mrs. Hall's hospitality and kindly thoughtfulness on these occasions. His family circle was ideally happy, and in all he did he was constantly supported by his wife. For her and her family deep sympathy will be felt by many friends. For forty-four years Donald Hall devoted his great gifts to his hospital, its patients, its nurses, and to many others. The gratitude and affection he inspired will not soon be forgotten.

## A. HEDLEY VISICK, F.R.C.S.

Mr. Arthur Hedley Visick died after a brief illness at York on April 4 at the early age of 51. He came of a medical family. His father was well known in North London as an anaesthetist, and on his mother's side he was related to Sir Albert Cook and the late Mr. J. Howard Cook, of Uganda. He was educated at Epsom College and St. Bartholomew's Hospital, gaining an entrance scholarship there in 1915. He

did not take up his studies, however, until 1918, as he served in the Army during the war. From the first Hedley Visick showed his interest in surgery. He won easily the Treasurer's prize and later the Foster prize for anatomy. In his final year he had the unusual distinction of being awarded the Walsham prize and the Brackenbury surgical scholarship as well as the Willett medal for operative surgery. He qualified in 1922, and served as house-surgeon first to Sir Holburt Waring and then to the ear, nose, and throat department at St. Bartholomew's. He graduated M.B., B.S. in 1924, and immediately afterwards took the F.R.C.S. He then gained valuable surgical experience as chief assistant to Sir Charles Gordon-Watson and demonstrator of anatomy at St. Bartholomew's. In 1926 he went to Michigan as an instructor in surgery at the university there. After this year in America he settled in York, and in due course was put on the staff of the York County Hospital and was made surgical specialist to the Military Hospital. He was also consulting surgeon to the York City Hospital and to a number of smaller outlying hospitals.

From his earliest days as a medical student Visick had set his heart on being a surgeon. Even before he qualified he used to watch surgeons at work in other hospitals. This he continued to do at all stages of his career: he would often come up to London for a few days for this purpose. He was a keen and regular member of the surgical travelling club to which he belonged. When Hedley Visick started in York it was as a general practitioner, but he gradually did more surgery, gave up general practice completely, and quickly built up a reputation not only in York but in a wide area around the city as a first-rate surgeon. At first he interested himself in thyroid surgery, but over the last ten years he became especially expert in gastric surgery and was well known for his work on this subject. As a Hunterian professor at the College of Surgeons last year he lectured on gastrectomy, and he contributed to this and other journals a number of thoughtful and valuable articles on the surgery of peptic ulcer. His follow-up clinic was a model of completeness in detailed record-keeping. Every Wednesday, with medical and radiological colleagues, he personally saw all the patients who attended this clinic. Each interview and examination was quick and informal but thorough. Each patient was called by his Christian name and was glad to come. In his earlier days Visick was an unusually good teacher, while in later years he showed the same ability as a lecturer.

One of Hedley Visick's characteristics was his great and genuine enthusiasm for any subject he took up. This was combined with an excellent pair of hands, which made his operating a pleasure to watch. He was a man of even temper who greatly delighted in meeting old friends and making new ones. He was highly esteemed by his colleagues, and from 1938 to 1943 he acted as chairman of the York Division of the B.M.A. The place he made for himself as a consulting surgeon in York will not easily be filled. He was very happy with his family at his old house at Fulford and at his cottage in the country. The sympathy of all his colleagues and friends will be given to his wife and three children.

### MAURICE SORSBY, M.D., F.R.C.S.Ed.

Dr. Maurice Sorsby, who died at Los Angeles on April 6 at the age of 50, qualified M.B., Ch.B. at Leeds in 1922, proceeding M.D. in 1925. In the same year he also obtained the Edinburgh F.R.C.S. Devoting himself to otolaryngology, he held staff appointments at the Metropolitan Ear, Nose and Throat Hospital, the London Jewish Hospital, and the Plaistow Children's Hospital. He was also for a time consulting ear, nose, and throat surgeon to the L.C.C. hospitals. A sound early training in general surgery turned his interest mainly to the intracranial complications of ear disease and to the general aspects of the cancer problem. His study of the incidence of cancer in Jews, embodied in his excellent *Cancer and Race*, was a valuable contribution to a subject on which previously there had been more opinions than critical data. This detailed study of the incidence of cancer in Jewish communities in different parts of the world showed that the total cancer rate in Jews was everywhere approximately the same as that of the general population, though the distribution according to the organs affected varied considerably. These latter differences could in most cases be explained by environmental factors. The low incidence of cancer of the tongue, for instance, could be correlated with a low incidence of syphilitic leucoplakia, which so often precedes it. Maurice Sorsby's study on Beethoven's deafness was characteristic of his wide interests, and a busy professional career still left him time for much social activity. As a president of the London Jewish Hospital Medical Society he was largely instrumental, together with the late Dr. M. D. Eder, in forming the Emergency Medical and Dental Association for the relief of victims of Nazi persecution in the years before the war. A large circle of friends will feel sympathy with his widow and his two sons.

## Medico-Legal

### DAMAGES FOR A DOCTOR

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Dr. L. M. Billingham, of Great Waltham, Chelmsford, was run down by an Army vehicle on Nov. 28, 1947, and suffered serious injuries, including a fractured pelvis. He had previously worked in general practice and as a radiologist; as a result he was physically unfit for general practice but not for radiology.

In the action which he brought in the High Court against the driver and the War Office, Mr. Justice Croom-Johnson awarded him £4,000 damages for pain and suffering and £20,000 compensation for estimated loss of earnings for the remainder of his working life. This amount was computed on the basis of £2,000 loss of earnings for each of fifteen more years, less £10,000 to allow for contingencies, his increased earnings as a radiologist, and the large capital sum down which he was to receive. The defendants appealed on the ground that the damages were excessive, and that the judge had failed to take into account the fact that the plaintiff's fees would have been reduced by taxation.

Lord Justice Tucker, giving judgment[1] in the Court of Appeal, said that the judge could not have given sufficient weight to the fact that the doctor could now devote the whole of his time to radiology. The court thought the amount awarded for loss of earning capacity should be halved, making the total damages £14,000 instead of £24,000.

On the second point, that the judge had failed to allow for the reduction of the doctor's fees by income tax, his lordship said that this argument had been rejected twice by High Court judges sitting alone but had never come to the Court of Appeal for decision. It had been accepted in a Scottish case, but he thought with respect that it was fallacious. The principle of *restitutio in integrum* required that the doctor should be put in the same position *vis à vis* his patients as that in which he would have been but for the fault of the defendants—that is, that he should receive his fees in full. Questions of ultimate liability to the Revenue did not concern the defendants, though different considerations might arise in cases of P.A.Y.E.

Lord Justice Singleton, agreeing, said that general damages for loss of future earnings would not be subject to income tax, but that in assessing them no reduction should be made in respect of the tax which would have been payable on such earnings. He thought that cases of P.A.Y.E. would be in the same position. Mr. Justice Birkett concurred.

This action, incidentally, is a reminder of the convenience of the reform introduced by the Proceedings against the Crown Act last year, whereby a Government department can now be sued in the same way as a subject of the King, and the cumbrous procedure by petition of right is no more.

[1] *The Times*, March 11, 1949.

H.M. Customs and Excise state that from April 5 preparations appearing in the *National Formulary*, whether or not compounded with substances appearing in the monographs and formularies of the other publications specified in Provision 1 of Notice 78 M, or with an excipient, vehicle, base, or preservative, are exempt from purchase tax so long as they comply with the remaining provisions of Notice 78 M or 78 N.

# Universities and Colleges

## UNIVERSITY OF OXFORD

The George Herbert Hunt Travelling Scholarship for 1949 has been awarded to Derek Rawlins Wood, B.M., of Brasenose College.

## UNIVERSITY OF ST. ANDREWS

Chairs in Child Health and in Public Health and Social Medicine are to be established in the University as a result of the offer of the James Mackenzie Institute for Clinical Research, St. Andrews, to provide capital sums of over £15,000 for their endowment. Two years ago the assets of the institute, founded by Sir James Mackenzie in 1919, were realized and invested, and, after the transfer of the above sum to the University, the balance will be allowed to accumulate so that further projects may be considered in due course. Both the new Chairs will bear the name of Sir James Mackenzie.

## UNIVERSITY OF GLASGOW

Postgraduate lectures in ophthalmology will be delivered in the Department of Ophthalmology of the University on Wednesdays, May 4, 11, 18, and 25, at 8 p.m., and the general arrangements will be similar to the series held last year. A discussion will follow each lecture. Details will be published in the diary column of the *Journal* week by week.

## UNIVERSITY OF DURHAM

Professor C. F. M. Saint, sometime Professor of Surgery in the University of Capetown, will deliver the fifth Rutherford Morison Lecture at the Royal Victoria Infirmary, Newcastle-upon-Tyne, on Thursday, May 12, at 5.15 p.m. His subject is "The Morison Approach to Hydatid Disease."

## UNIVERSITY OF LONDON

Nicholas Henry Martin, B.M., B.Ch., M.R.C.P., has been appointed to the University Readership in Chemical Pathology tenable at St. George's Hospital Medical School from April 1.

Dr. E. W. R. Steacie, Director of Division of Chemistry, National Research Council of Canada, gave the first of three lectures on "Gas Phase Reactions of Organic Radicals" at King's College, Strand, W.C., on April 21. He will deliver the second lecture to-day (Friday, April 22) and the third on Monday, April 25, at 5.30 p.m.

A lecture on "Bacteriophage and Antibiosis" will be delivered by Professor A. Gratia, Professor of Parasitology and Bacteriology in the University of Liége, at the London School of Hygiene and Tropical Medicine, Keppel Street, W.C., on April 25 at 5.30 p.m.

Professor Kl. Gollwitzer-Meier, of the University of Hamburg, will deliver a course of three lectures on physiology at King's College, Strand, W.C., on May 13, 16, and 18 at 5.30 p.m.

A course of two lectures on "Applications of Polarography to Medicine" will be delivered by Dr. Rudolph Brdička, Associate Professor of Physical Chemistry in Charles University, Prague, at Westminster Medical School, Horseferry Road, S.W., on May 24 and 26 at 5.30 p.m.

All the above lectures are addressed to students of the University and to others interested in the subjects. Admission is free, without ticket.

The following candidates have been approved at the examination indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN MEDICAL RADIOLOGY (THERAPY).—*Part I*: R. J. Dickson, P. K. Dutt, E. W. Emery, Frances A. Fouracres, N. D. M. Harvey, H. B. Morris, A. W. Reghers, B. Strickland.

### UNIVERSITY COLLEGE

The following lectures, admission to which is free, without ticket, will be given in the physiology theatre of University College, Gower Street, W.C.: April 25, May 2, 9, 16, 23, and 30, and June 8 and 13, at 4.45 p.m., "Selective Toxicity, with Special Reference to Chemotherapy," by Professor Adrien Albert (Australian National University); May 3, 10, and 17, at 5.15 p.m., "Physiological Properties of Ethyl Alcohol," by Dr. M. Grace Eggleton; May 31 and June 7 and 14, at 5.15 p.m., "Muscular Contraction," by Professor A. V. Hill, F.R.S.; June 2, 9, 16, and 23, at 4.45 p.m., "Some Aspects of Nitrogen Metabolism in the Mammal," by Dr. J. S. Bach.

## UNIVERSITY OF LEEDS

Professor G. Grey Turner will deliver the Moynihan Lecture in the Riley-Smith Hall of the University Union on Monday, April 25, at 3 p.m. His subject is "Moynihan and the Training for Surgery." Members of the medical profession are invited to attend the lecture.

## ROYAL COLLEGE OF PHYSICIANS OF IRELAND

On April 5, with Dr. Bethel Solomons, President in the chair, the Honorary Fellowship of the College was conferred on Baron Boyd-Orr, F.R.S. The oration was delivered by Dr. T. P. C. Kirkpatrick, Registrar of the College. Baron Boyd-Orr then delivered a lecture on "Medicine in a Changing World." A vote of thanks was proposed by Dr. P. Moran, President of the Medical Association of Eire, and seconded by Dr. A. R. Parsons, Senior Fellow of the College, and was passed by acclamation.

The following candidates have been admitted Licentiates in Medicine and Midwifery, having passed the Final Examination in Medicine, Surgery, and Midwifery of the Conjoint Board of Ireland:

J. G. Campbell, C. A. Cusack, J. J. Dollond, M. M. Marks, C. W. R. Murray, J. B. McCaffrey, W. J. McKeogh, Joan M. O'Connell, E. J. M. O'Connor, F. J. O'Hagan, E. O'Rafferty, Julia O'Reilly, W. P. Timmon.

# Medical Notes in Parliament

### Foreign Visitors and the N.H.S.

Sir WALDRON SMITHERS on April 8 raised the question of National Health Service Leaflet No. 2. The cover of this promised to provide all medical, dental, and nursing care for visitors to this country, whether of British nationality or not, no insurance qualifications being necessary. Sir Waldron said he understood that the pamphlet was available to all visitors on arrival in this country. He pointed out that the National Health Service Act, 1946, declared that the duty of the Minister of Health should be to promote the establishment of a comprehensive health service to secure improvement in the physical and mental health of the people of England and Wales. He did not find in the Act any permission to the Ministry of Health to offer medical services free to the whole world. Sir Waldron said he had received letters asserting that people came here, got false teeth and spectacles, and then went to Antwerp or Amsterdam and sold them. A French doctor told him that patients who could afford the fare from Calais went over for treatment. He asked the Minister how many foreigners had taken advantage of these services and at what cost.

Dr. HADEN GUEST asked whether Sir Waldron had any evidence of large-scale improvident supply of wigs, artificial teeth, and other things to people coming from abroad. He suggested Sir Waldron's protest was frivolous.

Mr. KENNETH LINDSAY thought the leaflet embodied an excellent idea. He hoped to see the Ministry of Health make the Service reciprocal and suggested a start with Belgium. Western Union should extend to the whole of the social services.

Mr. BLENKINSOP, replying for the Ministry of Health, said one of the virtues of the National Health scheme was that, so far as the patient was concerned, little red tape and form-filling were required. Sir Waldron Smithers's proposal would require an elaborate organization. The legality of the issue was provided for in Sections 3, 27, 33, 38, and 41 of the Act. There was no invasion of our shores by persons anxious to obtain glasses, false teeth, wigs, artificial limbs, and so on. Similar fears had been expressed when the National Insurance Act was introduced in 1911. There had then been stories about false teeth being sold in the bazaars of the East. Up to date 750,000 copies of the leaflet had been printed and 170,000 distributed. He could not give the number of foreigners treated under the National Health Service Act, because the Ministry did not intend to discriminate between one section of the people who were in the country and another. To get the statistics Sir Waldron Smithers wished would require completion of difficult forms and would require people of all nationalities inside this country to submit to examination about their nationality. Regulations of that kind would cost more than the minor provision now being made. Americans, Canadians, and others who had experienced the value of the service provided expressed themselves delighted. He agreed with what Mr. Kenneth Lindsay had said. Last year some 633,000 foreign visitors had come to these shores. Assuming that they stayed about a month—which was too long an average—and made the average use of the Service which was made by the ordinary population—which, again, was unlikely—the cost would run at something like £200,000 a year. That sum should not arouse any anxiety. The Government was satisfied that for the small expenditure involved it was doing good service to friends of this country throughout the world.

### Reciprocity

Mr. HUGH FRASER on April 7 asked what Mr. Bevan intended to do for members of the Merchant Navy who, although contributors to the National Health Service, were unable to make full use of the benefits of that Service.

Mr. BEVAN said that merchant seamen, like anyone else who went abroad, were unable to obtain treatment under the National Health Service Act while out of this country. The Government intended to negotiate reciprocal arrangements with other countries wherever the opportunity arose. He thought that one such arrangement was being negotiated at the moment.

No. 13

# INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended April 2.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

*Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for:* (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

| Disease | 1949 | | | | | 1948 (Corresponding Week) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | (a) | (b) | (c) | (d) | (e) | (a) | (b) | (c) | (d) | (e) |
| Cerebrospinal fever | 30 | 5 | 16 | 4 | 2 | 51 | 6 | 35 | 1 | 2 |
| Deaths | | — | 1 | | | | 1 | 1 | | |
| Diphtheria | 105 | 16 | 28 | 3 | 4 | 161 | 23 | 46 | 12 | 1 |
| Deaths | 1 | — | — | — | — | 3 | — | 1 | — | — |
| Dysentery | 62 | 5 | 23 | 3 | — | 188 | 14 | 38 | 1 | — |
| Deaths | | | | — | — | | | | — | — |
| Encephalitis lethargica, acute | — | — | — | 1 | — | 1 | — | 1 | — | — |
| Deaths | | — | | | | | — | | | |
| Erysipelas | | | 25 | 4 | 4 | | | 37 | 9 | 3 |
| Deaths | | — | | | | | — | | | |
| Infective enteritis or diarrhoea under 2 years | | | | 51 | | | | | 31 | |
| Deaths | 30 | 1 | 2 | — | 1 | 40 | 4 | 6 | — | — |
| Measles* | 15,819 | 1487 | 396 | 154 | 151 | 10,874 | 1719 | 295 | 90 | 53 |
| Deaths† | | | — | — | — | | | 3 | — | — |
| Ophthalmia neonatorum | 29 | 5 | 12 | — | 1 | 72 | 4 | 22 | — | — |
| Deaths | | | | | | | | | | |
| Paratyphoid fever | 2 | — | 1(B) | — | — | 1 | — | 1(B) | — | — |
| Deaths | — | — | — | — | — | — | — | — | — | — |
| Pneumonia, influenzal | 1,481 | 58 | 21 | 10 | 12 | 764 | 44 | 3 | 13 | 7 |
| Deaths (from influenza)‡ | 274 | 20 | 6 | 1 | — | 15 | 2 | 1 | — | — |
| Pneumonia, primary | | | 210 | 37 | | | | 263 | 27 | |
| Deaths | 333 | 45 | | 8 | 14 | 214 | 35 | | 7 | 13 |
| Polio-encephalitis, acute | 2 | 1 | | | | 4 | — | | | |
| Deaths | | | | | | | | | | |
| Poliomyelitis, acute | 13 | 1 | — | — | — | 15 | — | 2 | 1 | — |
| Deaths§ | 2 | — | | | | 4 | 1 | | | |
| Puerperal fever | | — | 9 | | | | 1 | 18 | | — |
| Deaths | | | | | | | | | | |
| Puerperal pyrexia‖ | 110 | 6 | 5 | 1 | — | 123 | 7 | 12 | — | — |
| Deaths | | — | | | | | — | | | |
| Relapsing fever | — | — | | | — | — | — | | | — |
| Deaths | | | | | | | | | | |
| Scarlet fever | 1,257 | 87 | 186 | 80 | 43 | 1,421 | 108 | 305 | 46 | 43 |
| Deaths† | | | — | — | — | | | 1 | — | — |
| Smallpox | — | — | — | — | — | — | — | — | — | — |
| Deaths | | | | — | — | | | | — | — |
| Typhoid fever | 1 | — | 1 | 1 | — | 5 | — | — | 1 | 1 |
| Deaths | — | — | — | — | — | — | — | — | — | — |
| Typhus fever | — | — | — | — | — | — | — | — | — | — |
| Deaths | | | | — | — | | | | — | — |
| Whooping-cough* | 2,998 | 247 | 276 | 121 | 64 | 2,639 | 166 | 22 | 52 | 13 |
| Deaths | 13 | 2 | 1 | 1 | — | 11 | 1 | 1 | 1 | — |
| Deaths (0–1 year) | 280 | 37 | 45 | 21 | 8 | 344 | 48 | 33 | 21 | 20 |
| Infant mortality rate (per 1,000 live births) | | | | | | | | | | |
| Deaths (excluding still-births) | 6,101 | 814 | 644 | 211 | 158 | 4,777 | 730 | 620 | 183 | 103 |
| Annual death rate (per 1,000 persons living) | | | 12·9 | 13·1 | | | | 12·5 | 11·4 | |
| Live births | 7,927 | 1272 | 1028 | 441 | 258 | 8,659 | 1351 | 1191 | 377 | 289 |
| Annual rate per 1,000 persons living | | | 20·6 | 27·3 | | | | 24·0 | 23·6 | |
| Stillbirths | 205 | 29 | 23 | | | 232 | 26 | 34 | | |
| Rate per 1,000 total births (including stillborn) | | | 22 | | | | | 28 | | |

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales, Eire, and Northern Ireland.

# EPIDEMIOLOGICAL NOTES

## Smallpox

As was anticipated in these notes (April 9, p. 640), there have been further cases of smallpox following the infection and death of a passenger on the s.s. *Mooltan*. Among the persons exposed to infection while on board the following secondary cases have been reported. The notifying authority and the date of onset of illness are given in each case: Port of London, 3.4.49; Paddington M.B., 5.4.49; St. Pancras M.B., 5.4.49; Isle of Axholme R.D.C., 5.4.49; Paddington M.B., 6.4.49; Liverpool C.B., 6.4.49; Wembley Borough, 7.4.49; Sutton and Cheam Borough, 7.4.49; Torquay Borough, 8.4.49; Aylesbury Borough, 12.4.49; and Richmond Borough, 12.4.49. There is still some uncertainty about the diagnosis in patients reported from Southwark M.B. and Abertillery. In many other persons who travelled on the s.s. *Mooltan* and who subsequently came under observation the suspicion of smallpox has not been confirmed. The above list contains information available up to April 19, when all the confirmed cases of smallpox in England and Wales had been in contact on the s.s. *Mooltan* and should therefore be considered as imported cases. In other words, there have so far been no secondary cases infected in this country. These are expected to appear at any time.

The disease is a severe form of variola major. Five of the patients have died, two of them in the prodromal stage. The disease has been haemorrhagic in some; with others there has been extreme modification resulting from vaccination.

## Suspected Smallpox

Two patients are under observation at Laceby Smallpox Hospital. They are in no way associated with the s.s. *Mooltan*, and furthermore the diagnosis is uncertain. They come from Brigg and Bolton-on-Dearne and were taken ill on April 13 and 14, respectively.

## Discussion of Table

In *England and Wales* increases were recorded in the notifications of measles 512 and dysentery 28. There were decreases in the incidence of scarlet fever 100 and acute pneumonia 66.

After declining for four weeks the incidence of measles rose; the rise was mainly confined to the Home Counties. The largest increases in the notifications were Middlesex 260, London 213, Yorkshire West Riding 111, and Surrey 107; the largest decreases were Staffordshire 189 and Leicestershire 147.

A small decrease in the number of notifications of scarlet fever was recorded in most areas of the country; the only notable exception was a rise in Essex due to 62 cases in Billericay U.D. There were only very small fluctuations in the local trends of diphtheria. The only large variations in the local incidence of whooping-cough were rises in London 66 and Warwickshire 51.

No new outbreaks of dysentery were reported during the week. The increased incidence was due to scattered cases; 18 counties notified the presence of a case compared with 9 counties in the preceding week.

In *Scotland* an increase was recorded in the number of notifications of measles 56, whooping-cough 32, and scarlet fever 13. There were decreases in the incidence of acute primary pneumonia 32 and diphtheria 12. The rise in the notifications of scarlet fever was mainly due to the experience of the south-eastern area, and the decrease in the incidence of diphtheria occurred in the western area.

In *Eire* there were rises in the incidence of measles 36 and of diarrhoea and enteritis 15 and a fall of 20 in the notifications of scarlet fever. There were 28 cases of measles notified in Donegal, Stranorlar R.D.; otherwise these changes were mainly due to the experience of Dublin C.B.

In *Northern Ireland* the only appreciable change was a fall of 27 in the notifications of measles, due to a small decrease throughout the country.

## Week Ending April 9

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,191, whooping-cough 2,608, diphtheria 106, measles 14,724, acute pneumonia 1,093, cerebrospinal fever 39, acute poliomyelitis 14, dysentery 63, smallpox 4, paratyphoid 5, and typhoid 1.

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Charter Travelling Scholarships, value £300 for one year, have been awarded by the Pharmaceutical Society to Miss Joan Mary Rhodes, B.Pharm., Ph.C., of Worthing, to enable her to study the conditions of pharmaceutical practice in Denmark, and also, subject to his passing the final examination for the B.Sc. (Pharm.) Degree of the University of Manchester in the summer of 1949, to Robert Guest Baker, of Manchester, to study in New York. The Charter Travelling Scholarship was founded in 1943 to mark the 100th anniversary of the granting of a Royal Charter to the Society.

# Medical News

### Blood Test for Cancer

At the annual meeting of the American Association for Cancer Research, which was held in Detroit last week, Professor Charles B. Huggins, of the University of Chicago, is reported by the *Manchester Guardian* (April 18) to have described a blood test for cancer. The test is said to be based on a change in the coagulability of the serum of patients with cancer, "due to a disturbance in the albumin content." It is positive not only in cancer, but also in tuberculosis, lobar pneumonia, meningitis, and other acute infections. Associated with Professor Huggins in this work were Dr. G. M. Miller and Dr. E. V. Jensen.

### Central Midwives Board

At its April meeting the Central Midwives Board re-elected Mr. Arnold Walker as chairman and Mr. J. P. Hedley as vice-chairman for the ensuing year.

### American Conference on Handicapped Children

A conference sponsored by the Child Research Clinic of the Woods Schools, Langhorne, Pennsylvania, was held on April 22 to discuss the effect on handicapped children of the emotional attitudes of parents and such environmental influences as school, church, and community. The conference programme was under the direction of Dr. Charlotte E. Grave, Director of the Woods Schools Child Research Clinic.

### Linctus Diamorphinae

There is no linctus diamorphinae in the new *National Formulary*, which will replace the *National War Formulary* as from May 1. Pharmacists will therefore be unable, under the Dangerous Drugs Regulations, to dispense the *War Formulary* preparation unless the formula is written out in full. To overcome this difficulty the Pharmaceutical Society has released its formulae for the two linctuses which are scheduled for inclusion in the *B.P.C. 1949*, which has not yet been published. A notice of their composition appeared in the *Pharmaceutical Journal* of March 26. They are linctus diamorphinae *B.P.C.* (the same strength as the *N.W.F.* linctus but with a different base), and linctus diamorphinae et hyoscyami *B.P.C.* After May 1, therefore, when a doctor prescribes linctus diamorphinae or linctus diamorphinae *N.W.F.*, pharmacists will dispense linctus diamorphinae *B.P.C.* unless a formula is written out in full.

### Victor Horsley Memorial Lecture

The Victor Horsley Memorial Lecture is held triennially and is usually given about the time of Sir Victor Horsley's birthday, which is in July. The lecture this year will be delivered by Sir Hugh Cairns, K.B.E., D.M., F.R.C.S., Nuffield Professor of Surgery, Radcliffe Infirmary, Oxford. The lecture will be in December, under the chairmanship of Dr. F. M. R. Walshe, and the exact time and place will be announced later.

## COMING EVENTS

### Royal Medico-Psychological Association

A meeting of the Child Psychiatry Section of the Royal Medico-Psychological Association will be held at the Royal Society of Medicine (1, Wimpole Street, London, W.) to-day (Saturday, April 23), at 11.15 a.m., when Dr. E. Mildred Creak and Dr. Richard H. Dobbs will read papers on "The Psychiatric Aspects of Maternity and Child Welfare Work." At 2.15 p.m. papers will be read by Miss Anna Freud and Dr. A. G. Watkins on "Effects of Hospitalization on the Child." Members of the British Paediatric Association, the Section of Paediatrics of the Royal Society of Medicine, and the Maternity and Child Welfare Section of the Society of Medical Officers of Health are invited to attend the meeting.

### Edinburgh Lectures

A series of Honyman Gillespie Lectures in association with Edinburgh postgraduate courses will be given in the Anatomy Theatre, University New Buildings, Teviot Place, Edinburgh, on Thursdays, at 5 p.m., from April 28 to June 9 (except May 19). The lectures are open to all graduates and senior students, and details will be published week by week in the diary column of the *Journal*.

### Care of Cripples

The Central Council for the Care of Cripples will hold a conference on "Planning the Future for the Physically Handicapped" on Friday, April 29, at the Conway Hall, Red Lion Square, London, W.C.1. Speakers include Mr. H. Osmond Clarke and Dr. G. S. Wigley. Information may be obtained from the Secretary of the Central Council, 34, Eccleston Square, London, S.W.1.

### Wright-Fleming Institute of Microbiology

The following course of six Almroth Wright Lectures on "The Bacterial Cell" has been arranged for the Summer Session, 1949. They will be given in the Lecture Theatre of the Institute at St. Mary's Hospital on Tuesday afternoons at 5 p.m. May 3: Professor E. W. Rideal, F.R.S., "Surface Properties of Bacteria." May 10: Mr. E. F. Gale, Ph.D., "Biochemical Properties of the Bacterial Cell Wall." May 17: Mr. W. T. J. Morgan, F.R.S., Ph.D., "Bacterial Antigens." May 24: Dr. M. R. Pollock, "Bacterial Nutrition." May 31: Mr. F. C. Bawden, F.R.S., "The Nature of Plant Viruses." June 7: Dr. A. S. McFarlane, "Electron Microscopy of Bacteria and Viruses." These lectures are open to all members of the medical profession and to all students in medical schools, without fee.

### St. George's Hospital Medical School

A series of lecture-demonstrations will be held in the large lecture theatre of St. George's Hospital Medical School (Hyde Park Corner, London, S.W.) on Thursdays, at 4.30 p.m., from May 5 to July 7, both dates inclusive. The series is open to all medical practitioners and senior medical students, without fee. Details will be published in the diary column of the *Journal* week by week.

### Musical Recital

A recital on behalf of the Princess Tsahai Memorial Hospital will be given by the St. Michael's Singers on May 11 at 6 p.m. at the Church of St. Michael, Cornhill, London, E.C.3. More than half the equipment for the Memorial Hospital, which has been built at Addis Ababa by means of British subscriptions, has been shipped from England. More is still required, and donations will be gratefully received. They should be addressed to the Honorary Treasurers, Lord Horder and Lord Amulree, c/o H. Reynolds and Co., 1, Bloomsbury Court, London, W.C.1.

### Royal Medical Benevolent Fund

The annual general meeting of the Royal Medical Benevolent Fund will be held at 11, Chandos Street, Cavendish Square, London, W., on Friday, May 13, at 5.15 p.m., with the President, Lord Webb-Johnson, in the chair. The statement of accounts for 1948 will be presented and officials and committee of management elected for the ensuing year.

## SOCIETIES AND LECTURES

#### Friday

LONDON UNIVERSITY.—At King's College, Strand, W.C., April 22, 5.30 p.m., "*Gas Phase Reactions of Organic Radicals*," by Dr. E. W. R. Steacie, Director of Division of Chemistry, National Research Council of Canada.

#### Saturday

BRITISH ASSOCIATION OF ALLERGISTS. At Medical Institution, Mount Pleasant, Liverpool, April 23, 11.15 a.m.; (1) "*The Management of Some Allergic Manifestations of the Upper Respiratory Tract*," by Dr. R. Donald (Melbourne); (2) "*Asthma in Childhood—Experiences in a Liverpool Play Clinic*," by Dr. C. A. Clarke; (3) "*Some Aspects of Nasal Allergy*," by Dr. E. Travers; (4) "*The Skin Reactions—Its Uses, Limitations, and Standardization*," by Dr. D. B. Macauley; (5) "*The American Approach to Allergy*," by Dr. A. E. Bernstien.

#### Monday

HUNTERIAN SOCIETY.—At Talbot Restaurant, 64, London Wall, E.C., April 25, 7 for 7.30 p.m., dinner and annual general meeting. "*Speech Defects and Voice Affectations*," address by Mr. H. St. John Rumsey.

LEEDS UNIVERSITY.—At University Union (Riley-Smith Hall), April 25, 3 p.m., "*Moynihan and the Training for Surgery*," Moynihan Lecture by Professor G. Grey Turner.

LONDON UNIVERSITY.—(1) At King's College, Strand, W.C., April 25, 5.30 p.m., "*Gas Phase Reactions of Organic Radicals*," by Dr. E. W. R. Steacie, Director of Division of Chemistry, National Research Council of Canada. (2) At London School of Hygiene and Tropical Medicine, Keppel Street, W.C., April 25, 5.30 p.m., "*Bacteriophage and Antibiosis*," by Professor A. Gratia (Liége).

LONDON: UNIVERSITY COLLEGE.—At Physiology Theatre, Gower Street, W.C., April 25, 4.45 p.m., "*Selective Toxicity with Special Reference to Chemotherapy*," by Professor Adrien Albert.

WESTMINSTER HOSPITAL SCHOOL OF MEDICINE, Meyerstein Lecture Theatre, Horseferry Road, London, S.W.—April 25, 5.30 p.m., Discussion: "*Cerebral Aneurysms*," clinico-pathological meeting.

#### Tuesday

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330-332, Gray's Inn Road, London, W.C., April 26, 2.30 p.m., "*Malignant Diseases and Radiotherapy*," by Mr. W. A. Mill.

#### Wednesday

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—At 28, Portland Place, London, W., April 27, 3.30 p.m., "*Occupational Eye Diseases and Injuries*" (2) Illustrated, by Mr. Joseph Minton.

**Thursday**

EDINBURGH UNIVERSITY.—At Anatomy Theatre, University New Buildings, Teviot Place, April 28, 5 p.m., "*A Workshop for Severely Disabled Men*," Honyman Gillespie Lecture by Professor T. Ferguson.

FACULTY OF RADIOLOGISTS: THERAPY SECTION.—At British Institute of Radiology, 32, Welbeck Street, London, W., April 28, 8.15 p.m., Sylvanus Thompson Lecture by Dr. F. Gordon Spear.

MEDICO-LEGAL SOCIETY.—At 26, Portland Place, London, W., April 28, 8.15 p.m., "*Medico-Legal Aspects of the Problems of Everyday Dental Practice*," joint paper by Surgeon Lieutenant-Commander John Bunyan, R.N.V.R., and Mr. C. W. Stidson Broadbent.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—April 28, 5 p.m., "*Stomatodaeal Ruminations, Clinical and Non-clinical*," Hunterian Lecture by Professor Charles F. M. Saint (late Professor of Surgery in the University of Capetown).

**Friday**

FACULTY OF RADIOLOGISTS: THERAPY SECTION.—April 29, joint meeting with Section of Radiology, Royal Society of Medicine. Discussion: "*The Method of Presentation of Results in the Treatment of Cancer.*" (1) At Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., 2.15 p.m., to be opened by Professor B. W. Windeyer and Drs. J. S. Fulton and Percy Stocks. (2) At Royal Society of Medicine, 1, Wimpole Street, London, W., 8.15 p.m., to be delivered by Dr. Ralston Paterson, Miss M. C. Tod, and Professor R. McWhirter.

KENT AND CANTERBURY HOSPITAL, Canterbury.—April 29, 5 p.m. to 7 p.m., clinical meeting.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, London, W.—April 29, 8 p.m., "*Reiter's Disease*," by Dr. A. H. Harkness.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—April 29, 5 p.m., "*Spondylolisthesis*," Hunterian Lecture by Professor R. I. Harris, Professor of Orthopaedic Surgery in the University of Toronto.

ROYAL INSTITUTE OF PHILOSOPHY.—At University Hall, 14, Gordon Square, London, W.C., April 29, 5.15 p.m., "*The Relevance of Psychical Research to Philosophy*," by Professor C. D. Broad.

## APPOINTMENTS

Mr. J. L. B. Ansell has been appointed Surgeon-Apothecary to his Majesty's Household at Sandringham in succession to Sir Frederic J. Willans, K.C.V.O., deceased.

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DONOVAN, W. T., M.B., Ch.B., D.P.H., Medical Officer of Health, Metropolitan Boroughs of Bethnal Green and Poplar.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—*Chest Physician, Peterborough Area:* G. B. Royce, M.B., Ch.B. *Medical Superintendent, Hellesdon Hospital:* F. J. Napier, M.B., B.S., D.P.M. *Ophthalmic Surgeon, Peterborough Area:* G. M. Barling, M.B., Ch.B., D.O.M.S. *Specialist Obstetrician, Peterborough Area:* Norman Kimbell, M.B., Ch.B., M.R.C.O.G. (*Corrected announcement*).

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LOGAN, DANIEL CRAWFORD, M.B., Ch.B., D.P.H., Medical Officer of Health, Whittlesey, Cambridgeshire.

## BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

**Halle.**—On March 21, 1949, at Sheffield, to Frances and Hugh, a daughter—Elizabeth Anne.

**Hulbert.**—On April 5, 1949, at West Hill Hospital, Dartford, to Elizabeth, wife of K. F. Hulbert, F.R.C.S., a daughter.

**O'Sullivan.**—On April 11, 1949, Una (née O'Leary), wife of Dr. J. G. O'Sullivan, Manchester, a daughter.

**Pooler.**—On April 10, 1949, at Easterholme, Stretton, Derbyshire, to Pamela (née Relton), wife of H. E. Pooler, M.B., D.A., a brother for Rosamund.

**Taylor.**—On April 11, 1949, in Edinburgh, to Helena (née Lauder Thomson, M.B., Ch.B., D.P.H.), wife of Dr. A. W. O. Taylor, M.R.C.P.Ed., 9, Frogston Road East, Edinburgh, a son.

**Whalley.**—On March 10, 1949, to Joy (née Brooks), wife of Dr. G. Hamilton Whalley, Newcastle, a son.

DEATHS

**Burn.**—On April 10, 1949, at Bryansburn House, Bangor, Co. Down, Mrs. Alice M. Burn, M.B., Ch.B.Ed., D.P.H.

**Cuthbert.**—On April 7, 1949, at a nursing-home, Glasgow, Charles Campbell Cuthbert, M.D., M.B., Ch.B., formerly of 3, Buckingham Terrace, Glasgow, W.2, and his wife Jean Copeland.

**Davies.**—On April 6, 1949, after a short illness, John Christopher Davies, M.B., B.Ch.

**D'Esterre.**—On April 12, 1949, at Westwinds, 31, Alleyn Park, West Dulwich, S.E.21, William Henry Daniel Patrick D'Esterre, M.D., B.S., M.R.C.S., L.R.C.P., aged 79

**Groome.**—On April 10, 1949, at Canterbury, Walter Groome, M.B.E., M.B., C.M., aged 81.

**Mackay.**—On April 12, 1949, at Rockbank, Campbeltown, Argyll, Duncan Matheson Mackay, M.D.Ed., aged 79.

**Neill.**—On April 9, 1949, at Coonoor, South India, the Rev. Charles Neill, M.A., M.B., formerly of Craigavad, Co. Down, aged 80.

**Sorsby.**—On April 6, 1949, at Los Angeles, Maurice Sorsby, M.D., F.R.C.S.Ed.

**Wacher.**—On April 11, 1949, peacefully after a long illness, Harold Wacher, M.D.

# Any Questions?

*Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.*

### Penicillin–Phthalylsulphathiazole Antagonism

**Q.**—*The National Formulary, 1949, on page 13 states that "there is evidence that it [phthalylsulphathiazole] should not be given with penicillin." Would you please quote the evidence?*

**A.**—Poth, Wise, and Slattery (*Surgery*, 1946, **20**, 147) gave phthalylsulphathiazole to six patients and succinyl sulphathiazole to five patients to reduce the coliform organisms in the large bowel. Penicillin was then given intramuscularly (20,000 units at two-hourly intervals) while the administration of the sulphonamide was continued. There was no demonstrable effect on the reduced flora induced by succinylsulphathiazole, but there was an abrupt and significant increase in the coliform flora in all the cases treated with phthalylsulphathiazole. The phenomenon could not be explained. The authors recommend that penicillin should not be administered simultaneously with phthalylsulphathiazole if it is important to maintain a reduction in the coliform flora of the bowel, as in the treatment of chronic coliform infections of the urinary tract or ulcerative colitis.

Streicher (*J. Amer. med. Ass.*, 1947, **134**, 339) in an investigation on the effect of orally administered penicillin in chronic ulcerative colitis found that the antibacterial effect of penicillin was impeded by the administration of phthalylsulphathiazole. The organisms studied were *Bacterium coli, Staphylococcus albus*, and streptococci of gamma type. When 3 g. of phthalylsulphathiazole was given in addition to 225,000 units of penicillin by mouth, 300 units of penicillin was needed to inhibit the *Bact. coli in vitro* as compared with 20 units when the penicillin was given alone. Nevertheless, Streicher considers that in practice oral penicillin and phthalylsulphathiazole may be combined with advantage. More recently Stewart and Jones (*Ann. trop. Med. Parasit.*, 1948, **42**, 33) have studied the effects of combining penicillin and phthalylsulphathiazole in the treatment of experimental amoebic infection in the rat. Both drugs were effective prophylactically, with a possible additive effect. Therapeutically, phthalylsulphathiazole enhanced the action of penicillin without itself having any effect on the established infection.

There is thus no definite confirmation of the observations reported by Poth and his co-workers suggesting that the combined use of penicillin and phthalylsulphathiazole is undesirable in clinical practice, but until further evidence is available succinyl sulphathiazole would appear to be a wiser choice in combined therapy.

### Xanthomatous Biliary Cirrhosis

**Q.**—*What are the features of the condition known as "primary biliary xanthomatosis"?*

**A.**—"Primary biliary xanthomatosis" is more often termed "xanthomatous biliary cirrhosis." It is a disorder in which chronic obstructive jaundice and hepato-splenomegaly are associated with cutaneous xanthomata (plana or tuberosa), and less frequently with xanthomata in the tendons, bones, or coronary arteries. The serum cholesterol level is greatly raised, owing mainly to an increase in the quantity of cholesterol ester. This uncommon condition is placed by Thannhauser in the group of hypercholesterolaemic primary essential xanthomatoses. This author's monograph (*Lipidosis: Diseases of the Cellular Lipid Metabolism*, 1940, Oxford University Press) contains a full bibliography and should be consulted.

### Petroleum Products and the Skin

**Q.**—*Can you give any information on the reactions which may occur when one of the following is applied to the skin: (a) light liquid paraffin. (b) liquid paraffin B.P., and (c) soft paraffin (yellow or white)?*

**A.**—Light liquid paraffin, liquid paraffin *B.P.*, and soft paraffin (yellow or white) do not usually give rise to any

reaction when applied to intact skin, even for prolonged periods. These oils collect in the mouths of the hair follicles, and, when their use in association with cosmetics is accompanied by insufficient attention to skin cleansing, aggregates of oil and particulate matter may give rise to mechanical plugging of the follicle opening. The occurrence of follicular hyperkeratosis, comedones, and sometimes pustular eruptions has been recorded following the use of impure paraffin oils in hair oil (*Year Book of Dermatology and Syphilology*, 1946, p. 277) and also as a result of the application of impure petroleum jelly (yellow soft paraffin). It is likely that the hyperkeratotic reaction in such instances is due to the presence of aromatic hydrocarbons which the refining process has failed to remove. This defect should not occur in medicinal preparations. The introduction of even highly refined paraffins into the subcutaneous tissues gives rise to an oleogranuloma, and consequently this must be borne in mind when application of these oils to damaged skin is considered. The ill effects of paraffin oils on damaged or diseased skin are otherwise due to their physical properties. In general it is undesirable to apply paraffin oils to skin which is inflamed or weeping, as they retain the heat, fail to mop up the exudate, and thus render the skin moist and soggy—a condition in which it is especially liable to infection.

### Safe Dose of Acetylsalicylic Acid

**Q.**—*What is the largest dose of acetylsalicylic acid that can be taken within twelve hours without endangering health?*

**A.**—The amount of acetylsalicylic acid which can be taken with safety varies for different people. Single doses of 20 g. (300 gr.) have been fatal, and some susceptible persons have had a severe allergic reaction after 0.6 g. (10 gr.). The principal danger is from haemorrhage, owing to a fall in the blood prothrombin level. If this is counteracted by giving menaphthone beforehand it is probably safe to take from 5 to 10 g. (75 to 150 gr.) in 12 hours.

### Dyspareunia

**Q.**—*A woman aged 28 has always had severe pain on intercourse. She is normally developed, and no structural abnormality of uterus, ovaries, or parametrium can be felt. Endometrial biopsy also shows no abnormality. The pain can be elicited only by moving the cervix, but is not felt when the uterus is squeezed without being moved. The patient also complains of frequency of micturition, and has had bouts of mild pyrexia. A recent abortion has not altered the pain. Any advice on this problem would be welcome.*

**A.**—Tenderness of the cervix and the production of pain on moving that organ strongly suggest the presence of disease in the cervix or neighbouring tissue. The other clinical features of this case also point to a diagnosis of chronic cervicitis. If this is deep-seated in the glands, and there is no superficial evidence of it, it may be difficult to exclude. The presence or absence of intermenstrual discharge should help. If chronic cervicitis is present, treatment with surgical diathermy or a graduated course of medical diathermy should be tried. Another possibility is endometriosis in the pouch of Douglas or utero-sacral ligaments; even intermittent pyrexia can be associated with this. For this condition another pregnancy should be encouraged, and if it progresses satisfactorily spontaneous retrogression of the endometriosis might occur. In either of the above conditions, if the pain proves intractable, injection of the paracervical ganglia with a local analgesic is sometimes useful. If no organic disease is present the discomfort might be explained by a congenitally short vagina which exposes the vault and the cervix to an unusual degree of trauma during coitus, or by an inherent hypersensitivity of the cervix. There might also be a psychogenic basis leading to aversion to coitus.

### Pig as Vector of Ascaris

**Q.**—*Is there a greater risk of human infection with roundworm from vegetables grown in soil containing pig manure as compared with other manures? How long do the ova remain viable in manure, and is there any means of destroying them?*

**A.**—In spite of the fact that the roundworm (*Ascaris suis*) occurring in the pig is morphologically indistinguishable from the roundworm (*Ascaris lumbricoides*) occurring in man, it does not normally develop to maturity in the human host, although it has been shown that *A. lumbricoides* may reach maturity in the pig if the animal is placed on a vitamin-deficient diet. The pig cannot therefore be regarded as a reservoir for human ascariasis, but it is believed that pigs play a part in the dissemination of eggs of *A. lumbricoides* which have been ingested previously with human faeces. The ova of *Ascaris* commonly remain viable in buried manure for at least a year, although much longer periods have been recorded. During this resting period they are very resistant to chemicals, but may be destroyed by drying, and perish almost immediately if heated to 55° C.

### Thickening of Palmar Skin

**Q.**—*An unmarried female aged 49, well developed and active, is greatly distressed by the formation on both palms of a thickened, dry, rough skin with a tendency to crack and fissure. The condition appears to be hyperkeratosis. What is the treatment?*

**A.**—A diagnosis is necessary before suggesting treatment in this case, and cannot be made without more knowledge of the patient's general condition, menstrual history, past medical and dermatological history, and family history. The condition might be psoriasis, lichen simplex, constitutional eczema, lichen planus, or keratodermia climactericum, among other things. A patchy hyperkeratosis of palms and soles is occasionally associated with the climacteric and is responsive to oestrogen therapy. Treatment should be undertaken with care, starting probably with 0.5 mg. of stilboestrol daily. It should not be carried to the point of provoking uterine haemorrhage if the periods have stopped. It would, perhaps, be advisable to submit the case to a dermatologist for clinical review before undertaking treatment.

### Intravenous Calcium Chloride and Gluconate

**Q.**—(*a*) *I understand that intravenous calcium chloride is dangerous to the digitalis-controlled heart. Does this apply to the rapid intravenous injection of calcium gluconate to determine the circulation time?* (*b*) *Have fatalities been recorded with this drug, or with ether, saccharin, dehydrocholic acid ("decholin"), or magnesium sulphate?* (*c*) *Which is the safest?*

**A.**—(*a*) There are numerous reports, both clinical and experimental, on the synergic effects of calcium chloride with digitalis; and fatalities have been recorded in animals and in human beings. On the other hand, many observers have used calcium gluconate without any fatal result in large numbers of patients suffering from serious cardiovascular disease which was fully controlled by digitalis (Goldberg, *Amer. J. med. Sci.*, 1936, **192**, 36; Baer and Slipakoff, *Amer. Heart J.*, 1938, **16**, 29; Berliner, *Amer. J. med. Sci.*, 1936, **191**, 117). H. C. Wall (*Amer. Heart J.*, 1939, **18**, 228) pointed out that calcium chloride contained three times as much calcium, weight for weight, as calcium gluconate; and in the former ionization was much greater. The rare fatalities in human beings occurred in extremely ill patients with advanced heart disease. In heart failure the blood volume is greatly increased and the circulation time slowed, these factors acting as safety-valves to the sudden rise of calcium concentration in the chambers of the heart, which apparently causes the fatal outcome (Mcguigan and Higgins, *J. Lab. clin. Med.*, 1938, **23**, 839). These factors, however, also tend to prevent a precise end-point being attained, and in patients with slow circulation time, and taking less than 5 ml. of calcium gluconate, no subjective sensation may be noticed. Thus, to be safe, intravenous calcium should be given slowly, but this would vitiate the result. Bernstein and Simpkins (*Amer. Heart J.*, 1939, **17**, 219) showed that magnesium sulphate had none of the dangers incidental to the use of calcium salts, and gave more exact readings at the slower circulation rates.

(*b*) No fatalities have been reported following the use of saccharin, dehydrocholic acid, or magnesium sulphate. Leinhoff (*J. Amer. med. Ass.*, 1935, **105**, 1759) reported a fatality accompanying the injection of 2.5 ml. of 10% ether in saline in a case of bronchial asthma. He doubted whether this was alone the cause of death, but felt that it was a precipitating factor. Hitzig advises against the injection of saccharin and ether into the same vein, because it may give rise to thrombosis and local pain. If the substances are injected outside the vein severe local reactions occur. The only untoward

effects reported after the use of dehydrocholic acid were in allergic or asthmatic patients. K. J. Norman (*Amer. Heart J.*, 1947, **34**, 740) mentioned three such cases, in one of which sensitization to the drug itself was acquired.

(*c*) Dehydrocholic acid, magnesium sulphate, and saccharin are safe, provided allergy is excluded in the case of the first named.

### Arcus Senilis

**Q.**—*What significance should be attached to the presence of a well-developed arcus senilis in a man aged 37, with normal blood pressure and without signs or symptoms of cardiovascular disease?*

**A.**—No significance should be attached to this. The writer has under his care one of a family in the members of which a definite arcus senilis develops at about the age of 16 years. The differential diagnosis is from the Kayser-Fleischer ring, which is coloured and is associated with hepatolenticular degeneration (pseudo-sclerosis and Wilson's disease).

### Oestrogen Therapy of Menorrhagia

**Q.**—*In the article on sex hormones in therapeutics (B.M.J., Jan. 29, p. 165) it is stated that intensive oestrogen therapy will control heavy and prolonged menstrual bleeding. What would be the most appropriate synthetic drug to use orally, and in what dosage?*

**A.**—The statement was made in reference to so-called functional uterine haemorrhage. Stilboestrol 1 mg., or ethinyl oestradiol 0.05 mg., orally every four hours, might be used. It is emergency treatment in that it controls the bleeding by raising the oestrogen level above the bleeding threshold. There is still the problem of preventing or controlling oestrogen-withdrawal haemorrhage, which is likely to occur when treatment is suspended.

### Ptyalism in Pregnancy

**Q.**—*A patient had excessive salivation all through her first pregnancy; she could not swallow the saliva but had to spit. Belladonna or sedatives failed to relieve the condition. She is now pregnant again and the salivation is returning. What treatment do you suggest?*

**A.**—The treatment of ptyalism in pregnancy is difficult because the aetiology is unknown. There is often, however, as in hyperemesis, a psychological underlay which manifests itself by the constant spitting—a conscious or subconscious dislike or fear of pregnancy. Usually the condition clears up by the time quickening is first felt, and this should be impressed on the patient. Calcium gluconate (10 ml. of 10% solution daily) has been given intravenously with good results in some cases. After a similar query was answered some years ago (April 14, 1945, p. 543) one correspondent advised putting very thin slices of lemon between the cheeks and the teeth. Another reported having successfully treated a patient with 20 drops of 25% benzyl benzoate in 90% alcohol taken in water every four hours.

### Treatment of Asthma

**Q.**—*A female patient of 43 has been subject to acute attacks of hay-fever from the age of 8. Six years ago she developed sharp attacks of asthma lasting several days, usually followed by bronchitis. The asthma has been successfully treated with subcutaneous adrenaline. Unfortunately, however, owing to the frequency of nocturnal mild attacks, I have for many months had to use maintenance doses as a suppressive, and in consequence the patient has become adrenaline-fast. She now complains of palpitation and cardiac pain, both during the severe attacks and for some weeks afterwards, despite prolonged rest in bed. A recent blood count showed R.B.C. 3,500,000 and W.B.C. 16,000 per c.mm., with a haemoglobin value of 75%. I am treating the anaemia with intramuscular injections of "anahaemin." Can you make any alternative suggestions for prophylaxis of the mild nocturnal attacks, and what treatment do you recommend during the violent attacks?*

**A.**—For the periodic violent attacks, when adrenaline fails, intravenous aminophylline, 0.48 g. in 20 ml., is usually effective. For alternative nightly prophylaxis one might suggest aminophylline 0.2 to 0.4 g. with or without phenobarbitone gr. ½ (32 mg.); if there is gastric irritation after aminophylline, enteric-coated aminophylline or glucophylline in similar doses might be tried, or the aminophylline could be given per rectum, 0.5 g. in 10 ml. of water, with a syringe and catheter; alternatively, "franol" (theophylline, ephedrine, and phenobarbitone), 1 or 2 tablets, might be tried, and a favourite prescription in such cases is "caffneine" 1 drachm (3.5 ml.) in water three times a day. This preparation is made up as follows:

| | | |
|---|---|---|
| ℞ | Caffeine sod. iodid. .. .. | 5 gr. (0·32 g.) |
| | Sod. iodid. .. .. .. | 5 gr. (0·32 g.) |
| | Dilute hydriodic acid .. .. | 5 m. (0·3 ml.) |
| | Decoction of coffee .. .. | 40 m. (2·4 ml.) |
| | Water to .. .. .. .. | 1 fl. dr. (3·5 ml.) |

The history and leucocytosis suggest the presence of infection. Is there infection in her sinuses?

### Washing-soda in Tea

**Q.**—*A patient who works in a buffet informs me that it is a widespread practice to put a handful of washing-soda in the tea urn at each filling to make the tea darker than the strength of the brew would warrant. Would the constant drinking of tea so treated be harmful?*

**A.**—It is not likely that any harm would come of the use of washing-soda in tea. But, as with other methods for making tea go further, the resulting drink is not nearly so good as it should be.

## NOTES AND COMMENTS

**Lactation.**—Dr. ARMIN RUTISHAUSER (Dessie, Wollo Province, Ethiopia) writes: In a question about lactation in virgins ("Any Questions?" Nov. 20, 1948, p. 925) it is stated that Margaret Mead describes how one of the savage tribes in New Guinea adopts babies who are then breast-fed by women who have never had children of their own. Before the war I spent two years at the hospital of Dr. Albert Schweitzer, French Equatorial Africa, where I saw the following two cases in the obstetrical department. There was one woman who gave birth to a child, but after a few days breast-feeding was impossible, as the breast did not produce any milk, though we had the baby suckling. All the treatment we undertook had negative results. Then I was asked permission to take mother and child away, as the family wanted to consult a sorcerer. I agreed, seeing that we were at a standstill. After some weeks the family came back—baby all right and mother producing a lot of milk. Another mother died, and her mother, a very old-looking woman with breasts like paper, started to feed the baby after having disappeared for a short time in the jungle. After those experiences my curiosity was aroused, and I found out that the women underwent treatment with the result that inactive breasts started to produce milk. During the following year we tried hard to find out what kind of plants were used for this special treatment, but it was quite impossible to get information, as the sorcerers are very anxious to keep their knowledge for themselves. In any case, it would be very interesting to learn more of all the drugs used in Africa, as I am quite sure that there are a great number of very important ones.

**Late Menopause.**—Dr. HILDA M. DENHOLM-YOUNG (Farningham, Kent) writes: Regarding menstruation at age 56 ("Any Questions?" April 2, p. 602), the question does not state if the woman was from Shetland or Orkney, where menstruation finishes normally at about 60 and where children are sometimes borne at that age.

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**Disclaimer.**—Mr. HAROLD DODD (London, W.1) writes: During the past week there have been several announcements in the public press with regard to my connexion with the Fife-Openshaw Nursing Home. These have been made in spite of my urgent requests. I begged the Press to confine their statement to the announcement made by Princess Arthur "that she was giving up her connexion with it." My wishes were ignored. Therefore I should be grateful if you would kindly insert this disclaimer.

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